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Isolation Effect in Mice (*Mus musculus*): (i) Does it Really Induce Aggression?

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Abstract — In previous studies, isolated mice are found to be extremely more aggressive than group-reared mice. In most of those studies, however, the pairings of the group-reared mice were randomly determined, without attention to individuals' ranks in their home cages. In this study, the effect of isolation was analyzed by comparing isolated mice with dominants of group-reared mice. In experiment 1 the group-reared mice were randomly chosen as in previous studies. Isolated mice were significantly more aggressive, but the pairings of the group-reared mice were found to be all dominant vs. subordinate. In experiment 2, the group-reared dominants encountered unfamiliar dominants in an unfamiliar place. Dominant mice were found to be less aggressive than the isolated mice. This result was inconsistent with the "territorial dominant hypothesis" on the hyperaggressiveness of the isolated mice. Sequential analysis of behavior clarified that the isolated mice had a sequential pattern quite different from the group-reared mice, and provided an illustrative figure for the "escalation hypothesis". The lack of aggression in the group-reared mice, however, left a question about the sequence similarity of aggressive behavior in isolated and group-reared mice.

There have been many studies on isolation rearing that concluded that isolation increased aggressiveness in mice (for example, King 1957; Kahn 1954; Ely & Henry 1974; Anton et al. 1968; Crawley et al. 1975; Goldsmith et al. 1976; Koyama 1985; Cairns & Nakelski 1971; Cairns & Scholz 1973). Several explanations have been proposed: the "escalation hypothesis" from the behavioral aspect (Cairns & Scholz 1973), an explanation considering endocrinal changes caused by isolation stress (Baer 1971; Valzelli 1973; Schwartz, Sackler & Weltman 1974), and a view that sees isolated mice as dominant and territorial (Brain 1975). Fox (1986) described an "isolation-emergence syndrome" (the behavior patterns characteristic to the animals when they were returned to social groups from isolated housing conditions) in dogs as (1) fear response, (2) hyperexploratory behavior, and (3) impaired pain perception. He also described, in the context of animal husbandry, how physiological changes occur in relation to the grouping condition.

On mouse research, however, there was a trend, as Valzelli (1973) had written, of concentrating on the aggressiveness increased by isolation rather than examining the "isolation syndrome" as a whole. Valzelli pointed out somatic, behavioral and neuro chemistric effects of isolation, and listed increased aggressiveness and inner tension, and decreased sexual activity, exploratory activity, learning ability, and memory consolidation processes as behavioral effects.

There were, however, few experiments on isolation effect in which the social rank of the group-reared mice was taken into consideration, until the recent studies of Benton et al. (1978), Mainardi et al. (1977) and Parmigiani et al. (1981).

Group-reared mice were traditionally encountered "randomly". There must, however, exist social rank order when individuals were kept together in a single cage and it could be easily expected that their home cage status might affect their responses to strange mice they met

in the test cage.

In the studies of Mainardi et al. (1977) and Parmigiani et al. (1981), the isolated mice were encountered with group-reared mice with known social rank. About two thirds of the dominants won against the isolated mice in both studies, leading to the conclusion that the dominants were more aggressive than the isolated mice. On the other hand, Benton et al. (1978) compared the physiological characteristics of the isolated mice with those of the dominants and subordinates, and concluded that the isolated mice had specific physiological characteristics.

The main purpose of the present study was to examine how the results would differ when the social relationships of the group-reared mice were taken into consideration in the encounter test. Experiment 1 was conducted comparing the behavior of the isolated mice with the group-reared mice with randomly determined encounter partners. In experiment 2, only the dominants of the group-reared mice were used as encounter partners.

Experiment 1

Methods

Subject

Subjects were 32 male ddY closed-colony mice (Saitama Laboratory Animal Supply Co.) bought at 3 weeks of age.

Housing condition

16 mice were socially isolated (Iso) and 16 were kept in pairs (G) from 3 weeks of age until the age of 15 weeks when they were tested in 8 pairs respectively. Food (Oriental Lab. Chow, MF) and water were offered ad libitum for all the mice. Room temperature was kept approximately at 20°C. Light was not controlled. Iso were kept individually in aluminum cages with 5 compartments. Each compartment was 13 × 23 × 12 cm, and the ceilings, floors, and front parts were wire meshed. G were paired in wire-meshed cages with 3 compartments, each compartment being 30 × 12 × 23 cm. Only the left and right compartments were used. The middle compartments were left empty with opaque partitions in the centers to obstruct exchanges of visual and tactile stimuli.

Periodical observations of behavior were made for G in home cages for 10 min once a week, and behaviors related to aggression were also checked whenever they were seen. These observations were done only to compare the results in experiment 1 with those of experiment 2.

Test procedure

At 15 weeks of age all the mice went through an encounter test. Each mouse met another mouse from the same housing condition in the test apparatus for 15 min. The test apparatus was a box (19 × 38 × 32 cm) with a removable partition in the center of the longer side. Four lateral parts of the box were made of acrylic resin and the floor was stainless steel with lines, which divided the base into 8 equal squares. There was no ceiling for the test apparatus. The color of the lateral parts differed for effective video recording from the front side. The colors were as follows: colorless transparent for the front, transparent dark brown for the left and right side, and opaque black for the back.

The encountering partners of Iso were determined randomly, and those of G were determined not only randomly but also double-blindly. At the begining of the encounter test, mouse body weights were measured. One of the mice was marked with blue and the other was stroked with a brush on the same part of the body. Each mouse was then put into either side of the test apparatus and was then left there for 5 min to explore the apparatus with the partition closed. After the exploration the partition was removed and the mice were encountered for 15 min. The encounter test was video recorded by a camera (Olympus color VX-304) 1 m away from the front side of the apparatus.

Behaviors were analysed for 3 factors: (i) the

activity measured by the amount of lines crossed by each mouse, (ii) the frequency and time length of 26 behavior patterns shown by each mouse, and (iii) inter- and intra-individual behavioral sequence patterns of the mice.

Twenty-six behavioral patterns recorded were: 《Non-social behaviors》 *Sty*: Staying. No locomotion, no apparent social behavior, and no movement that fell under other behavioral patterns, but not freezing. *Wlk*: Walking, but not following the other mouse. Sometimes accompanied by sniffing of the floor or the lateral part of the test apparatus. *Len*: Leaning against the wall. Standing up with forefeet touching the lateral part of the test apparatus. *Rer*: Rearing with forefeet in the air. *Sgr*: Self-grooming and face washing. *Def*: Carrying defecated objects in mouth. 《Social behaviors》 *Wch*: Watching the other mouse motionlessly. *App*: Approaching the other mouse (when the other mouse was walking, the behavior was designated as "following"). *Nsf*: Sniffing at the nose of the other mouse. *Gsf*: Sniffing at the genital area of the other mouse. *Snf*: Sniffing at the other mouse, but not at its nose nor its genital area. *Fav*: Quickly turning its face away in response to the social behavior by the other mouse. *Ret*: Stepping backwards in response to social behavior by the other mouse. *Flw*: Following. An approaching movement of one of the mice to the other when the other is walking. *Crw*: Crawling under the other mouse. *Frz*: Freezing in response to the social behavior by the other mouse, but not watching him. *Afr*: Freezing after the social behavior by the other mouse, but not watching him. *Put*: Putting forefoot or forefeet on the other mouse. *Gro*: Grooming the other mouse. *Igr*: Intensive grooming of the other mouse. *Atk*: Attacking. *Fgt*: Fighting. *Upr*: Showing upright posture. *Chs*: Chasing. Running after the other mouse when the other mouse is running away. *Kik*: Kicking. *Fle*: Fleeing, running away from the other mouse.

The behaviors of each mouse in the video tapes were recorded on data sheets. The starting times of each of the 26 behaviors were recorded at a precision level of 0.01 s at minimum. These records were for analysis of factor (ii) and (iii). Then the behavioral time tables of both mice were matched together to be used for analysis of inter-individual behavior.

Results

Activity

G mice showed an apparent decrease in activity during the 15 min test session. The decrease was significant in the first 6 min (Wilcoxon's Sign Rank Test, $T = 1$, $P < 0.005$), and activity stayed at the lowered level thereafter. Iso showed no significant change in activity during the test session. The activity level of Iso in the first 3 min was the same as in G (Mann Whitney U-test $T = 1.688$, $P > 0.05$), but maintained the activity level higher than G throughout the test session (Fig. 1).

Amount and Time Length of the Behaviors

The results of activity suggested that the behavior patterns that are most characteristic to the encounter situation would be seen in approximately the first third of the 15 min test session, so analyses were concentrated on the behaviors witin this period.

G showed non-social behaviors and some of the social behaviors significantly more than Iso (see Table 1).

Fgt was shown significantly more by Iso than G. Other behaviors that were also shown significantly more by Iso were Igr. Fle, Wch, Ret, Frz, Afr and Nsfs; Gsfs was very seldom in Iso.

Table 2 shows the amount of social behavior as a whole according to 3 patterns of engagement by the encountered mice. Social behavior was conducted by one or both of the mice. When a mouse began a bout of social behavior, there were several patterns possible until termination (an example is shown in Fig. 2). "Full social behavior" in Table 2 indicates a bout of social behavior from the beginning to the end (when both mice returned to non-social behaviors) indifferent of quality and quantity of changes of engagement pattern. In the case of Iso, both of the encountered mice engaged in

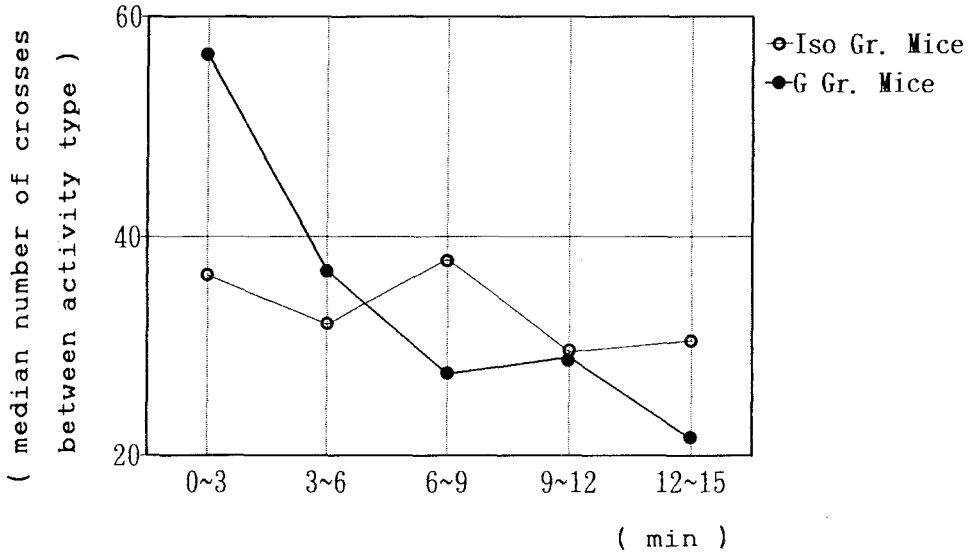

Fig. 1. Changes of activity during the 15 min encounter test.

Table 1. Medians of each behavior and results of Mann-Whitney U-test

Behavior	Iso	G	Result of U-test		
	(times)	(times)	Z value	Significance level	
sty	49	67	2.281	*	G > Iso
wlk	37	58.5	1.992	*	G > Iso
len	8.5	30	2.714	**	G > Iso
rer	7.5	17.5	2.974	**	G > Iso
sgr	1	3.5	2.048	*	G > Iso
def	0.5	1	N.S.		
wch	17.5	6	3.842	***	Iso > G
app	12	9.5	N.S.		
snf	23	29	N.S.		
nsf	5.5	2.5	2.088	*	Iso > G
gsf	0	2.5	3.224	**	G > Iso
fav	2	2.5	N.S.		
ret	3.5	1	2.539	*	Iso > G
flw	1	3	2.005	*	G > Iso
crw	0	0	N.S.		
frz	5.5	0	4.050	***	Iso > G
afr	1.5	0	3.019	**	Iso > G
put	0	0	N.S.		
gro	2.5	3.5	N.S.		
igr	0.5	0	2.732	**	Iso > G
atk	0	0	N.S.		
fgt	1.5	0	2.732	**	Iso > G
upr	0	0	N.S.		
chs	0	0	N.S.		
kik	0	0	N.S.		
fle	0	0	2.134	*	Iso > G

*: $P < 0.05$, **: $P < 0.01$, ***: $P < 0.001$, N.S.: not significant

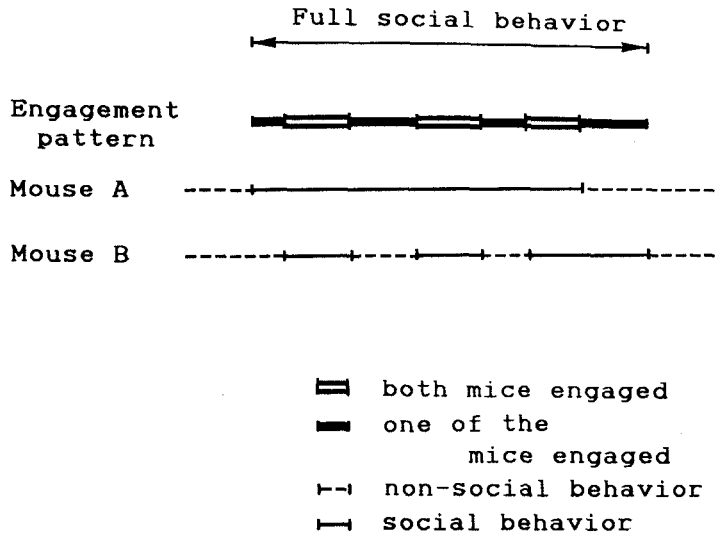

Fig. 2. An example of the engagement patterns into social behavior by 2 encountered mice.

social behavior significantly more frequently than G. The amount of the social behavior from only one of them did not differ and G had a higher frequency of full social behavior ($U = 9$, $0.05 < P < 0.10$).

The time lengths of the social behaviors were also compared according to the 3 patterns of engagement (Table 3). Iso engaged in social behavior together significantly longer than G. The bouts of full length social behaviors were also longer in Iso than in G. Social behaviors from either of the mice, however, were significantly longer in G than in Iso.

Sequential Analyses of Behavior

Intra-individual behavioral sequence: All the transition matrixes of each mouse were summed up in 2 transition matrixes of G and Iso. Figs. 3a and 3b show the flow of behaviors that were significant ($P < 0.05$) in cell-by-cell tests in G and Iso. Arrows indicate the direction of the sequence (arrow widths indicate the occurrence frequency). Both G and Iso had a huge circle of non-social behaviors constructed by Wlk, Len, and Sty, and there was a flow into social behavior only from Sty. The sequential pattern after the flow into social behaviors differed between G and Iso. Wch, App, and Snf were a center stage in both G and Iso. G showed Gro, Gsf, and a return to non-social behavior from Snf, Frz, and Gro to Rer, whereas Iso showed Gro, etc, and a trend towards aggression. There was only 1 return to non-social behaviors (from Gro to Rer) in Iso.

To get more simplified sequential flows, the behaviors were divided into 5 groups according to their natures. These groups are indicated as the squares of broken lines in the figures of sequences. Square I (NON-SOCIAL BEHAVIOR) is the square of non-social behaviors. II (APPROACH) is the square of the starting behaviors of social behaviors, i.e. the social behaviors that generally occur first and before direct interaction begins. III (SOCIAL EXPLORATION) is the square of social behaviors, including direct contact to the other mouse, but excluding aggressive behaviors. IV (AGGRESSION) is the square of aggressive social behaviors. V (RETREAT) is the square of behaviors quitting social interaction.

By this division, the arrows in the figure were subsequently classified into 2 types, i.e. intra-square and inter-square. Table 4 indicates the number and percentages of arrows in each square. The number of inter-square arrows of each square indicates the number of arrows that

Table 2. Social behavior according to engagement pattern

Behavior pattern	Iso	G	Results of U-test	
	(times)	(times)		
Both mice engaged	32	16	U = 0	Iso > G[1]
One of the mice engaged	67	53.5	N.S.	
Non-social behavior	36	44.5	N.S.	
Full social behavior[2]	37	44	N.S.	

1: $P < 0.001$, N.S.: not significant
2: See text for definition of "full social behavior"

Table 3. Time length(s) of social behaviors according to behavior pattern

Behavior pattern	Iso	G	Results of U-test		
				significance level	
Both mice engaged	3.3	1.12	U = 3	**	Iso > G
Either of the mice engaged	1.23	1.52	U = 6.5	*	G > Iso
Non-social behavior	3.21	4.11	U = 7	*	G > Iso
Full social behavior[1]	4.70	2.57	U = 5	**	Iso > G

*: $P < 0.05$, **: $P < 0.01$
1: See text for definition of "full social behavior".

"depart" from one square to another. The third row in Table 4 indicates the results of the dominant (Dom) mice in experiment 2 (which are explained later). The comparison of the upper 2 rows revealed that the distribution of percentages in each square was relatively similar except in square IV. In square IV, only 20% of the arrows were inter-square in Iso, whereas in G all were inter-square. The percentages of arrows that reaches square IV were also different between Iso and G (Iso, 35%; G, 7.7%).

Inter-individual behavioral sequence: A transition matrix was done for all pairs of behaviors that were shown by the 2 mice within 3 s. This means that every behavior of a mouse within 3 s after a behavior of the other mouse was operationally determined to be an inter-individual behavioral sequence in this analysis.

Two transition matrixes were made for the intra-individual analysis, except that there were (superficial) auto-transitional cells, in which the mice showed the same behavior in succession. Cell-by-cell tests were conducted on all of the cells of the 2 matrixes.

Using all of the behavioral sequences significantly shown ($P < 0.05$) by the mice, 3 sequential patterns were obtained in G (Fig. 4a) and Iso (Fig. 4b). Apparent difference in the sequential patterns was seen in pattern 3 of all mice. G showed Fav in response to Snf by the

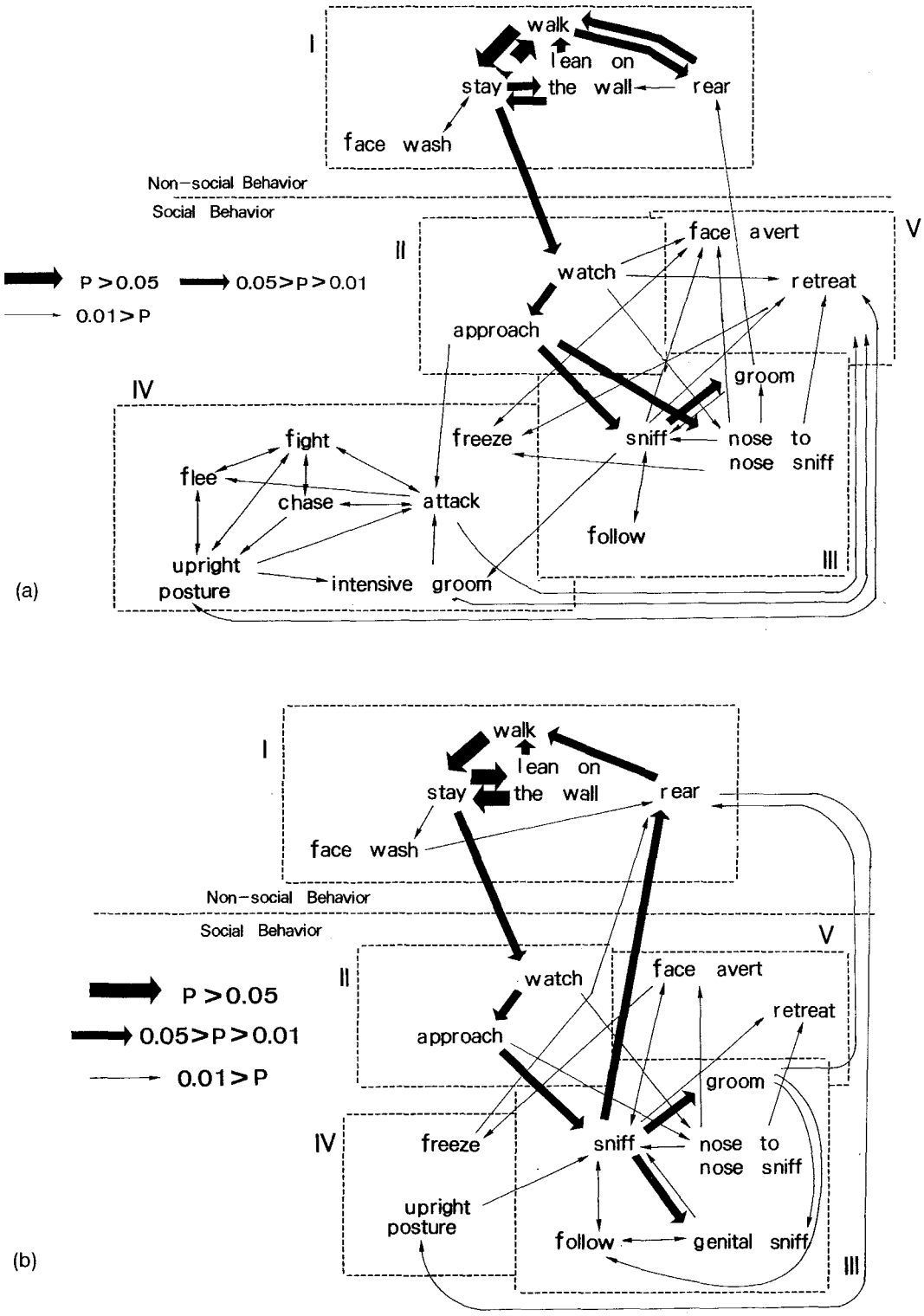

Fig. 3. Intra-individual sequential flow of behavior. (a) Iso mice. (b) G mice. Width of the arrows corresponds to the percentages of the frequencies each behavioral sequence occurred.

Table 4. Numbers and percentages of arrows that are related to each square.
Percentages indicate the proportion of inter- vs. intra-square arrows in each square and not the proportion to the total arrow number.

Square	I		II		III		IV		V		
Arrow type	Intra-Square	Inter-Square	Intra-Square	Inter-Square	Intra-Square	Inter-Square	Intra-Square	Inter-Square	Intra-Square	Inter-Square	Total
⟨Iso mice⟩ Number of arrows	10	1	1	6	6	7	16	4	0	3	54
%	90.9	9.1	14.3	85.7	46.2	53.8	80.0	20.0	0.0	100.0	
⟨G mice⟩ Number of arrows	7	2	1	3	10	6	0	2	0	2	33
%	77.8	22.2	25.0	75.0	62.5	37.5	0.0	100.0	0.0	100.0	
⟨Dom mice⟩ Number of arrows	8	4	4	4	11	7	0	1	2	3	44
%	66.7	33.3	50.0	50.0	61.1	38.9	0.0	100.0	40.0	60.0	

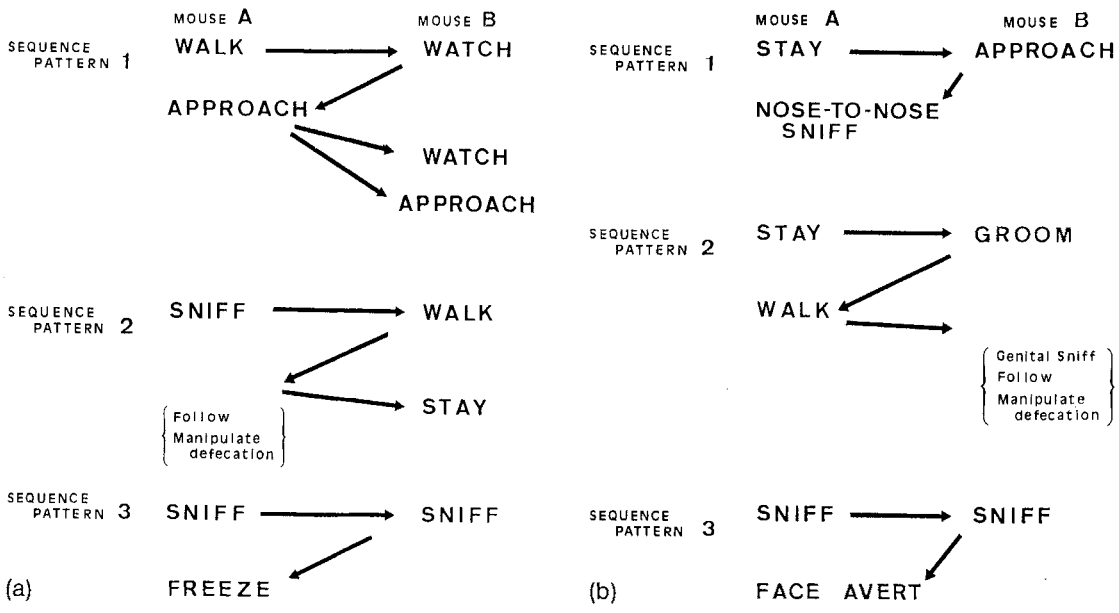

Fig. 4. Three patterns that were obtained as inter-individual sequential flow of behavior. (a) Iso mice. (b) G mice.

other mouse, whereas Iso showed Frz in the same sequential situation.

Discussion

Results of activity clearly showed the difference between isolated mice and group-reared mice. Isolated mice maintained high activity during the 15 min test session. This hyperactivity corresponds with that noted by Fox (1986), Valzelli (1973) and Essman (1966). This indicates that group-reared mice habituate to other mice in an unfamilier environment more easily than isolated mice.

I note 3 points after quantifying behaviors in the encounter situation of the G mice: (i) less aggression, (ii) longer lasting non-social behaviors, and (iii) longer oneway social behaviors. It can not be concluded from these results, however, that G mice are relatively indifferent to each other. They showed more Flw and full social behaviors than Iso mice. The results of behavioral sequence patterns may explain why the social behaviors of G mice were shorter than those of Iso mice. G mice showed more Rer than Iso mice, and they showed Fav in response to Snf of the other-mouse. It is possible that these behaviors might have the function of "cutting off" the social behavior from escalating into a more serious or high tension interaction. Chance (1962) suggested that "cut-off" acts, especially eye contact, were one of the social skills lowering inter-individual tension. One interesting point is that Rer is a behavior originally considered to be a non-social, place-exploring behavior. Whereas Fav was a behavior directly cutting social stimuli to and from the other mouse, the use of Rer at the end of social behaviors suggests that it also acquired an additional social cut-off meaning. This interpretation suggests the intentional use of Rer to cut off social interactions by pretending to be exploring, or as an (unintentionally shown) displacement activity which results in a cut-off function.

Behaviors of Iso mice were exactly opposite to those of G mice. Quantifying the behaviors of Iso mice, I noted the following 4 points; (i) more fights and behaviors related to aggression, (ii) more long-lasting social behaviors that were related to high tension and caution in both mice, (iii) more hyperactivity and lower adaptability, and (iv) less Gsf behavior. The difference in the distribution of percentages related to square IV in the intra-individual behavioral sequence suggests that, in Iso mice, there is a tendency in behavior to "center" about aggression, as in the so-called "behavioral sink" of aggression. This indicates that the characteristics of the Iso mice included not only their hyperaggressiveness, but also relatively few ways "out" from the aggressive behavior.

Another interesting point is that, although the Iso mice showed many long-lasting social behaviors including both mice, there were few Gsf behaviors. This result suggests the possibility that Gsf behavior had to be learned in the course of development in a social environment.

These results of G and Iso mice suggested the higher aggressiveness of the Iso mice, confirming previous studies. But inquiries in the pairing of G mice after the test clarified an interesting fact which must have affected the results. When G mice were used at the encounter test, the encountering partners were intentionally determined randomly and double-blindly. The inquiries revealed that all the pairings were of dominant and subordinate.

Group-reared mice were not aggressive in previous studies or in this experiment. The results of the pairing of G mice, however, brings about a question: can the group-reared mice be concluded to be not aggressive, or do the results only mean that, when a dominant encounters a subordinate, the group-reared mice are not aggressive? There is a possibility that dominants of the group-reared mice would be as aggressive as isolated mice if they were encountered with dominants.

Experiment 2

Experiment 2 was conducted in almost the same procedure as experiment 1 except that the encountering partners at the test were chosen in terms of social dominance in the group-rearing cages.

Methods

Subjects

Subjects were 36 male ddY closed-colony mice (Saitama Laboratory Animal Supply Co.) which were 3 weeks of age at the beginning of the experiment.

Housing Condition

All the mice were kept in pairs in the same cages that were used in experiment 1, and housing conditions were also the same.

Determination of Social Dominance

Procedures of observation were also the same as in experiment 1. Criteria for the social dominance in the home cages were as follows: *Dom-Sub Pair*: pairs in which attacks were mainly observed during the observation stage; *Dom-Dom Pair*: pairs in which fights were observed; *Sub-Sub Pair*: pairs in which aggressive behaviors were not observed.

Test Procedure

At 15 weeks of age 18 pairs of mice went through an encounter test. The test procedures of the test were as same as experiment 1. There were 3 kinds of pairings for the encounter test according to the dominance status: dominant vs. dominant, dominant vs. subordinate, and subordinate vs. subordinate. Only the results of the encounter of dominants vs. dominants are reported here.

Several changes were made in the behavioral patterns observed. The following behaviors were not counted in experiment 2: Def, Crw, Put, Kik (rarely observed in experiment 1), and Afr (included in Frz in experiment 2). In experiment 2, another behavior was additionally counted: Trn (turning to the other mouse).

Results

Social relationships in home cages

Of the pairs, 61.3% had apparent Dom-Sub relationships, about 29.0% were Dom-Dom, and the remnant were Sub-Sub. The Dom-Dom pairs showed not only fights but also attacks, and the change of the attacker was observed by 4/9 of the Dom-Dom pairs during the observation stage, which was not observed in the Dom-Sub pairs.

Amount of Behaviors

The amount of behavior by the dominants (Dom) was compared with the Iso mice of experiment 1.

Dom did not show aggression (Atk and Fgt) nor behaviors related to aggression except Frz. The difference was significant in Fgt and Igr (see Table 5).

Many non-social and social behaviors were shown significantly more in Dom than in Iso (Table 5). The difference was especially large in Sty, Snf, Gsf, Fav, and Flw (see Table 5).

Sequential Analysis of the Behaviors of Dominants

The results of the Dom mice went through the same procedure of intra-individual sequential analysis as in experiment 1. Fig. 5 illustrates the behavioral flow usually shown by Dom. There were thick lines from non-social behaviors (Sty and Len) to a social behavior (Trn). Social behavior started from Trn and returned to non-social behavior by 4 routes.

The numbers of intra- and inter-square arrows are listed in the bottom of Table 4. About 40% of the arrows were related to square III. There was only 1 inter-square arrow from square IV and no intra-square arrows in it.

Table 5. Medians of each behavior and results of Mann-Whitney U-test

Behavior	Iso	Dom	Result of U-test	
	(times)	(times)	Z value	Significance level
sty	49	84.5	3.824	*** Dom > Iso
wlk	37	63	2.572	** Dom > Iso
len	8.5	19	2.077	* Dom > Iso
rer	7.5	7.5	N.S.	
sgr	1	2	N.S.	
wch	17.5	17	N.S.	
app	12	20	1.945	(P < 0.10)
snf	23	52	3.923	*** Dom > Iso
nsf	5.5	10	2.506	* Dom > Iso
gsf	0	6.5	3.923	*** Dom > Iso
fav	2	16	3.956	*** Dom > Iso
ret	3.5	2	N.S.	
flw	1	6.5	3.528	*** Dom > Iso
frz	5.5	3.5	N.S.	
gro	2.5	4.5	N.S.	
igr	0.5	0	1.978	* Iso > Dom
atk	0	0	N.S.	
fgt	1.5	0	1.978	* Iso > Dom
upr	0	0	N.S.	
chs	0	0	N.S.	
fle	0	0	N.S.	

*: $P < 0.05$, **: $P < 0.01$, ***: $P < 0.001$, N.S.: not significant

General Discussion

Dom mice did not show aggression against unfamiliar Dom mice in the test cage. Iso mice were significantly more aggressive than the Dom mice. This was clearly different from the results of Mainardi et al. (1977) and Parmigiani et al. (1981).

As for the G mice, there were various routes including 1 thick line from social to non-social behavior in the sequential flow of the Dom mice. On the other hand, in the Iso mice there was only 1 thin line returning to non-social behavior. The distribution of percentages among the 5 squares was also highly similar between G and Dom mice. Overall, the results of Dom mice in experiment 2 were very similar to those of the G mice and different from those of the Iso mice in experiment 1.

The Iso mice also had a characteristic to "center" about aggression. The frequent use of cut-off behavior in the group-reared mice and the lack of it in the isolated mice, as mentioned in the discussion of experiment 1, may illustrate the behavioral mechanism that leads to such a "behavioral sink" of aggression. The isolated mice seemed to adhere to the social stimuli from the other mouse. This indicates that the isolated housing made the stimulus value of the other mouse so high that it was hard for the isolated mice to avert from the encountered partner. Another indication is that the isolated mice did not have a chance to learn how to use cut-off behaviors, whereas the group-reared mice had learned how they would effectively function to avoid unnecessary escalation of interaction with another animal. In other words, cut-off behavior might be one of the behaviors that is important as a social skill and that needs to be learned, like genital sniffing, in a social environment. The results on behavioral sequences clearly agree with the notion of the "escalation hypothesis" by Cairns & Scholz (1973) and proposes a concrete figure for it.

There have been several other explanations as to why the isolated mice are so aggressive.

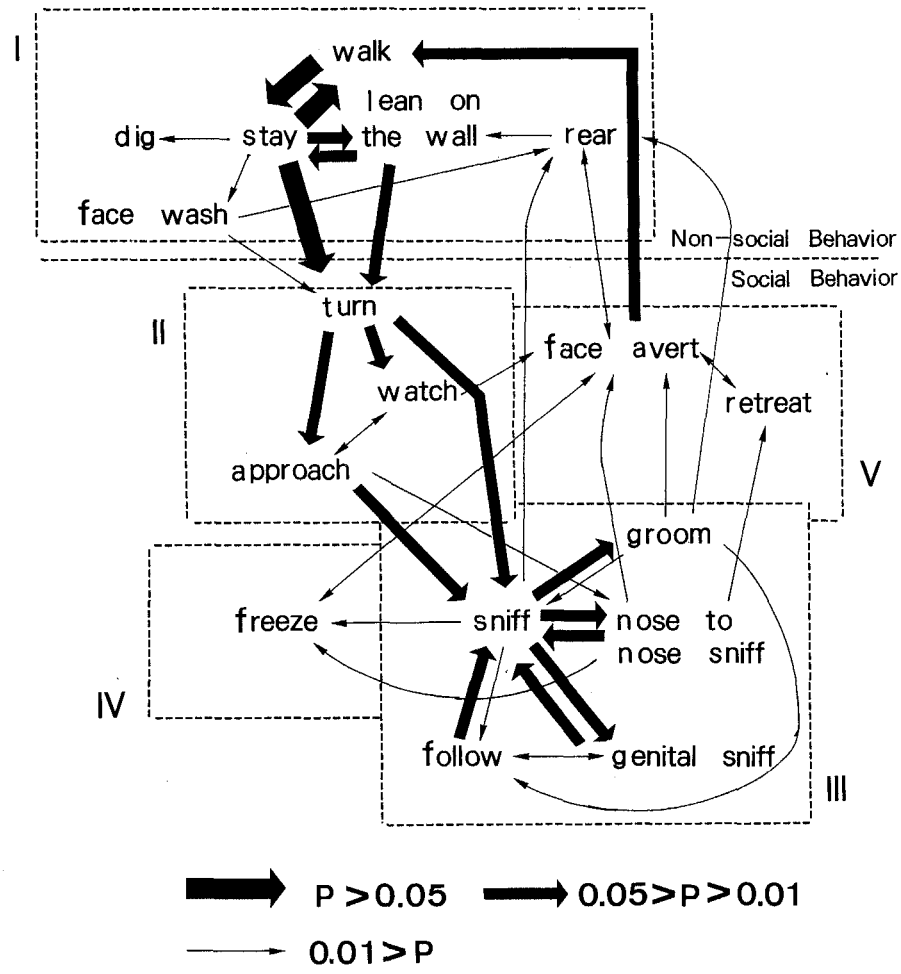

Fig. 5. Intra-individual sequential flow of behavior: Dom mice. Width of the arrows corresponds to the percentages of the frequencies each behavioral sequence occurred.

In a review Valzelli (1973) listed increased inner tension as a factor of the "isolation syndrome" in mice. According to Ramirez et al. (1980), excitement or irritation, states related to inner tension, cause aggressive behavior. In some studies it is suggested that isolated housing is stressful for mice (Schwartz et al. 1974; Weltman et al. 1968; Valzelli 1973) and causes such increased inner tension, whereas other studies suggested that it does not (Goldsmith et al. 1976, 1978b; Brain 1975; Stanislaw & Brain 1983; Anton et al. 1968). In these latter studies it was found that the isolated mice were not in a stressful condition when adrenal function was used as an index, and it was suggested that the isolated mice were territorial dominants. This denial of the stress hypothesis is, however, only a denial of the chronic stress due to individual housing and not of the acute stress possibly caused by the encounter test situation.

The results of experiment 2 showed that the isolated mice were different from dominant mice, and the result of hyperactivity in the isolated mice in experiment 1 suggested the possibility of their higher inner tension. A comparison of acute stress between mice from different housing conditions further illuminates isolation-induced aggression.

One of the questions that arises from the results in this study is whether the behavioral

sequence of the Iso mice is unique to isolated mice, or is it the sequence typically seen when aggressive interactions occur. As the group-reared mice did not show aggression at all, it was impossible to compare the aggressive behavior itself in group-reared mice with that of the isolated mice. So it is impossible to see whether it was behavior unique to the isolated mice or not, and there is still the possibility that aggression generally has a nature to "sink" once it occurs. Benton et al. (1978) concluded in their study that isolated mice had physiological characteristics of their own, which implies that their aggressive behavior would be different from that of the group-reared mice. The characteristics of the isolated mice need to be further clarified by such comparison.

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