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# Social Behavior, Dominance, and Social Deprivation of Rats Determine Drug Choice

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WOLFFGRAMM, J AND A HEYNE *Social behavior, dominance, and social deprivation of rats determine drug choice* PHARMACOL BIOCHEM BEHAV **38**(2) 389–399, 1991 —Relationships between social deprivation, dominance, and voluntary intake of ethanol (ETOH) and diazepam (D) were studied in male adult Wistar rats Social behavior was registered by tetradic encounters in the open field prior to the rats' drug experiences Social deprivation was induced by individual housing (LI) and contact caging (C) Nondeprived rats were housed in groups of four individuals (G) each Social deprivation facilitated ETOH intake, LI rats consumed 30% more ETOH than G Increase of deprivation by change of housing condition additionally raised ETOH consumption ETOH experiences did not affect subsequent D choice However, rats with a high ETOH consumption also preferred D. Individual drug disposition correlated with social dominance (in G to social activity) Even in individual isolation dominant rats took less drugs than subordinate ones, but these rats raised their ETOH consumption when the housing conditions were changed After nine months of voluntary ETOH intake and subsequently nine months without access to ETOH the rats showed signs of "behavioral dependence " Compared to naive animals they took twice as much ETOH and even after adulterating ETOH by quinine a high preference was perpetuated During this state modifying social factors were no longer effective

Social behavior Social isolation Social dominance Ethanol Diazepam Drug seeking Drug dependence

THE relevance of social variables for the drug-taking behavior of laboratory animals has been proved in particular for ethyl alcohol (ETOH). Short-term and long-term isolation enhance the consumption and alter the preference for alcohol concentrations in rats (9, 10, 24, 43, 45) and in rhesus monkeys (22). In these studies the animals were exposed to an experimental social situation which affected all individuals in the same way. Nevertheless, interindividual variation was remarkably high, suggesting that additional individual variables contribute to ETOH preference. An indication for such factors has been offered by experiments which additionally regarded social structures. The rank position of a male rat determined by his success in agonistic interactions influenced the voluntary intake of ETOH in rat colonies. Such results were interpreted as effects of social stress rather than as expression of endogenous individual states (2,13). A decision between the two possibilities requires a discrimination between rank positions without affecting the amount of social stress during drug exposition.

The procedure to establish a prediction of individual drug intake requires both a control of environmental social factors and a registration of the individual social behavior In the rat the first demand can be met by the housing conditions Complete social isolation for several weeks is obtained by single housing, the nondeprived state is reached by group housing, and an intermediate condition (selective motor deprivation) is achieved by "contact caging," enabling the animals to communicate through a grid of bars (45). Previous experiments showed that such housing condition affected drug intake, but there were no signs of dependence-like phenomena (45). A hypothesis to be tested is that in long-term experiments using the free-choice paradigm, additional temporal trends will develop which may lead to an irreversible state similar to psychic dependence in man.

The assessment of the individual social behavior before the first experiences with drugs can be performed by tetradic encounters (46,47). The advantage of putting four rats together into an open field instead of two (the dyadic case) is that the rat's behavior is not exclusively directed to one partner. Thus, a higher degree of variability and expression of individual spontaneous behavior can be observed Previous experiments with young male albino rats (Wistar) revealed the existence of social roles with regard to dominance and social activity (48) Such roles might contribute to the abovementioned individual variables influencing drug intake. The comparison between social behavior (without drugs) and later drug choice permits the testing of the hypothesis that dispositional factors for drug preference are reflected by the social behavior.

Compared to ETOH other psychotropic drugs (e.g , benzodiazepines) have hardly been studied with regard to the interaction between social variables and drug intake. Most of these investigations were only concerned with the effects of drug applications on the social behavior (14, 34, 36). A hypothesis to be tested can be that the intake of such drugs is affected by social variables in a similar way as in the case of ETOH [cf. (35)]. Similarities and differences in the effects of these drugs may indicate general or drug specific principles of drug preference, drug-seeking behav-

ior, and perhaps even the development of behavioral dependence (5, 6, 23, 28, 41, 42).

In this study, two psychotropic drugs are involved ethanol (ETOH) and diazepam (D). Although the two substances do not belong to the same class of compounds, they both exhibit biphasic patterns of action. In the low dose range excitatory, anxiolytic, and aggressive responses predominate, whereas in high dosages the drugs act as sedatives (8, 15, 26, 27, 31, 44). A further similarity is their potential to cause physical and behavioral drug dependence (16, 19, 25, 33).

The successive analysis of social behavior, ETOH choice and D choice in the same individuals enables not only the recognition of correlations between behavioral variables and drug-seeking behavior but also of interdrug relationships. The null hypothesis predicts that ETOH and D intake are independent of each other. Deviations from this hypothesis may either be due to a persisting influence of experiences with ETOH on the choice of diazepam or to individual (possibly dispositional) preferences concerning both substances

## METHOD

### *Animals and Housing*

All experiments were performed with male young Wistar rats (breeder. Hagemann, Lippische Versuchstierzucht, Extertal, West Germany). At the beginning of the experiments the body weights of the animals ranged from 120–140 g During the course of the experiments the body weight rose to 400–700 g.

Depending on the experimental situation the animals were housed in three different ways· a) group caging of four individuals in a Makrolon cage ($60 \times 38 \times 20$ cm); b) individual caging (Makrolon cage $43 \times 26 \times 15$ cm), c) contact caging involves four individually housed rats, however, the Makrolon cages were arranged in a square pattern such that grid bars enabled the rats to communicate with themselves.

Each cage was supplied with standard diet (Altromin 1324) ad lib The type of drinking fluid depended on specific experimental situation They were offered ad lib by means of (2–4) bottles with glass tubes.

At least three times a week, the consumption of food and fluid was measured and the body weights of the rats were determined. By such regular manipulations, the animals were familiarized to handling. Both the studies on drug-taking behavior and the behavioral tests were performed in air-conditioned rooms. The temperature was kept at $21 \pm 2$°C, the humidity ranged from 40 to 60% The light/dark cycle was set to LD 12 h/12 h (dark cycle starting at 6 p m.).

### *Tetradic Encounters*

Social and nonsocial behavior of the rats were assessed by tetradic encounter sessions in the open field prior to their first experiences with psychotropic drugs. The open field consisted of a black arena ($1 \times 1$ m) which was subdivided by white lines into 16 squares Each encounter lasted for 15 minutes during which four rats were put together into the arena. To enable a discrimination of the individuals by the observer the animals were marked on their back by means of colored dots The encounters were recorded on video tape by means of a video camera placed 2 m above the center of the open field. Encounter experiments always started 1–2 h after the beginning of the dark cycle when the circadian activity of the rats was high. The arena was diffusely illuminated by low intensive white light ($2 \pm 0.5$ lux).

### *Main Experimental Series ($n = 36$)*

This series consisted of a long-term choice of ETOH by rats housed under different social conditions (Table 1) Over a period of nine months drinking fluids containing 5, 10 and 20 vol.% ETOH were offered concomitantly in addition to tap water. The presentation of different concentrations was necessary since the preference for certain concentrations depends on prior experiences with ETOH (32,45). After an alcohol-free period of nine months ETOH choice was tested again. To detect possible signs of "behavioral dependence" the three ETOH-containing solutions were subsequently adulterated by the addition of increasing concentrations of quinine hydrochloride (0.05 g/l up to 0.35 g/l, increased by 0.05 g/l per week). Tap water was available and remained unchanged. The taste of quinine is aversive to the Norway rat (1,17), therefore, the rats are expected to prefer the quinine-free fluid (water) Since a "behavioral dependence" expresses itself in a strong demand for the drug ["craving," (41,42)], the aversion against quinine-adulterated solutions should be suppressed in ETOH-dependent animals.

During the period without ETOH an experiment lasting three months with diazepam (D) choice was included. The rats received two solutions of D (50 mg/l and 100 mg/l) in addition to tap water. The solutions were obtained by diluting the contents of diazepam Ratiopharm® ampoules with tap water Apart from diazepam, the ampoules contained solubilizing additives (per 100 mg diazepam· 300 mg benzyl alcohol, 20 mg benzoic acid, 980 mg sodium benzoate, 2.15 g ethanol).

Twelve of the 36 individuals which were kept under the same social conditions as the other rats received only tap water during the first nine months of the experiment. These "ETOH-naive" animals were compared to the "ETOH-experienced" rats; beginning with the phase of D choice and were treated like the other rats

To study the influences of stable and changing social conditions on long-term choice of alcohol, a time schedule of housing was established. At the beginning of the experiment the rats were divided into experimental groups of four animals each. Three of these groups of rats were housed individually (long-term isolation LI); another three in contact cages (C) and the last three in groups (G) During the whole course of the experiment G rats were separated once a week for 24 h in single cages to determine individual values of food, fluid and drug consumption and to study the effects of short-term isolation. Every 14 weeks the housing condition was changed according to a "circular" schedule G→C, C→LI, LI→G (Table 1). After two changes (28 weeks) the housing conditions were left constant until the end of the experiment.

### *Additional Series*

Apart from the psychoactive agent (ETOH or D) some drinking fluids contained additional constituents like quinine hydrochloride or D-solubilizing additives. To assess the influence of their taste on the choice of solutions three control series were performed. The first one ($n = 12$) aimed to estimate the influence of additives in D-containing solutions on fluid choice. D-free solutions of the additives (same concentrations as in the main series) were offered over a period of 14 weeks to G-housed, C-housed and LI-housed rats of the same age as those of the main experimental series receiving D-containing solutions

The two other series were performed to estimate the aversive effect of quinine. In the first one ($n = 8$), G rats received water and solutions with increasing concentrations of quinine (0.05–0.35 g/l) for seven weeks. In the second series ($n = 10$), the rats were presented with ETOH adulterated with 0.1 g/l quinine, nonadulterated ETOH and tap water for 2 weeks under LI housing During 14 weeks before the tests, the rats were presented ETOH (free choice), but in the last four weeks of this period the ETOH solutions were adulterated with quinine hydrochloride (0.1 g/l).

TABLE 1

LONG-TERM STUDY (102 WEEKS) OF VOLUNTARY DRUG CHOICE TIME SCHEDULE OF EXPERIMENTAL PHASES

| Weeks | Main Series | | | |
|---|---|---|---|---|
| −4–0 | C<br>water | LI<br>water | G<br>water | encounter experiments |
| 1–14 | C<br>ETOH* | LI<br>ETOH* | G<br>ETOH* | ETOH choice |
| 15–28 | LI<br>ETOH* | G<br>ETOH* | C<br>ETOH* | ETOH choice<br>after first change<br>of housing conditions |
| 29–42 | G<br>ETOH* | C<br>ETOH* | LI<br>ETOH* | ETOH choice<br>after second change<br>of housing conditions |
| 43–56 | G<br>water | C<br>water | LI<br>water | first drug-free<br>period |
| 57–70 | G<br>diazepam | C<br>diazepam | LI<br>diazepam | diazepam choice |
| 71–84 | G<br>water | C<br>water | LI<br>water | second drug-free<br>period |
| 85–91 | G<br>ETOH | C<br>ETOH | LI<br>ETOH | ETOH choice<br>(retest) |
| 92–98 | G<br>ETOH+quinine | C<br>ETOH+quinine | LI<br>ETOH+quinine | choice between water<br>and ETOH solutions<br>adulterated with quinine |

LI long-term isolation, C contact housing, G group housing Asterisks indicate periods during which ETOH-naive rats receive only tap water

*Evaluation of Housing Data*

The changes of body weight, food consumption, drug intake, concentration preference, and total fluid intake were established and submitted to linear interpolation to enable the calculation of means and standard deviations. The statistical analysis concerned two different aspects (a) the comparison among independent samples; and (b) repeated measurements. The tests of (a) used either temporal cross sections or temporal averages. Depending on the homogeneity of variances (Bartlett's test) ANOVA or nonparametrical tests (H-test, U-test) were used. The individual values of consumption by group housed rats were not directly available but were calculated from the total values measured for the group and the interindividual ratio of consumption during the 24-h periods of individual housing. Interdependences among different parameters were interindividually studied by means of linear regression and correlation procedures. Time courses (b) were assessed by means of trend analyses, ANOVA for repeated measurements, paired Student *t*-test, Wilcoxon's test, and Friedman's test.

*Evaluation of Behavioral Data*

Based on the video recording a simplified repertoire of behavioral patterns was established (48) which contained seven classes:

1. rest
2. ambulation
3. exploration
4. social investigation
5. play
6. aggression and aggressive play
7 submission and flight

By means of a two-step analysis the temporal succession of patterns was stored in a digital computer (HP 200). The first step comprised the interpretation of the behavioral sequence of each individual including his communicative partners by a trained observer using an audio tape. The interpretation was controlled by a second independent observer. The high positive correlation between the two evaluations ($r = +.98$) confirmed the reliability of the type attributions. During the second step the comments spoken on audio tape were stored in real time into the computer by use of a digital tablet ("bit pad one"). The time series were analyzed by means of computerized programs. The evaluations mainly concerned the temporal portions of the behavioral classes and the recipience of social communication A comparison among different groups required equivalent parameters. Since it cannot be presumed that this condition is matched for the relative portions of the behavioral classes, it is more adequate to use the "rank number" of the individual within his group in respect to the regarded parameter (e g , 1 for the most playful activity, 2 for the second most, etc.). Such rank numbers are then submitted to correlation analyses (48).

## RESULTS

*Initial Ethanol Choice (First Section· Week 1–14)*

The ETOH doses taken daily by the rats depended on the so-

TABLE 2

MEAN DRUG DOSES TAKEN BY RATS OF THE MAIN SERIES (ETOH g/kg/day, D mg/kg/day) DURING DIFFERENT PHASES OF THE EXPERIMENT (cf TABLE 1)

| | Daily Doses | | | Mean |
|---|---|---|---|---|
| ETOH 1st section | 1 57 (C) | 2 05 (LI) | 1 47 (G) | 1 70 |
| ETOH 2nd section | 1.73 (LI) | 1 86 (G) | 2 07 (C) | 1 89 |
| ETOH 3rd section | 1 78 (G) | 1 94 (C) | 2 36 (LI) | 2 03 |
| diazepam (ETOH-experienced) | 2 57 (G) | 2 20 (C) | 2 09 (LI) | 2 29 |
| diazepam (ETOH-naives) | 2 12 (G) | 2 32 (C) | 1 95 (LI) | 2 13 |
| ETOH last four weeks of the 3rd section (ETOH-experienced) | 2 02 (G) | 2 09 (C) | 2 38 (LI) | 2 16 |
| ETOH first four weeks of ETOH-retest (ETOH-experienced) | 3 32 (G) | 3 57 (C) | 3 83 (LI) | 3 60 |
| ETOH first four weeks of ETOH-retest (ETOH-naives) | 1 89 (G) | 1 27 (C) | 1 92 (LI) | 1 69 |

The letters in parentheses represent the housing condition, the mean intake summarize all individuals irrespective of housing

TABLE 3

MEAN RELATIVE PORTION OF ETOH TAKEN FROM THE 5 vol % SOLUTION BY RATS OF THE MAIN SERIES DURING THE COURSE OF THE EXPERIMENT

| | | | |
|---|---|---|---|
| ETOH-experienced | | | |
| 1st section | 37 36% (C) | 33.88% (LI) | 78 44% (G) |
| 2nd section | 28 12% (LI) | 36 53% (G) | 62 78% (C) |
| 3rd section | 32 90% (G) | 8 97% (C) | 63 73% (LI) |
| retest | 32 06% (G) | 26 31% (C) | 51 72% (LI) |
| + quinine | 5 58% (G) | 14 34% (C) | 16 61% (LI) |
| ETOH-naive | | | |
| retest | 75 33% (G) | 78 30% (C) | 79 82% (LI) |
| + quinine | 8 67% (G) | 23 90% (C) | 17 85% (LI) |

The letters in parentheses represent the housing condition

cial housing conditions. The highest quantity of ethanol was consumed by long-term isolated rats (LI) (2.05 g/kg/day). Contact-caged individuals (C) and group-housed rats (G) drank significantly less ETOH than LI animals, $F(2,21) = 3\ 74$, $p<0.05$. Differences between G (1.47 g/kg/day) and C (1 57 g/kg/day) were not significant (Table 2). Apart from the total quantity, the preferences for ETOH concentrations (5, 10, 20 vol.%) were also affected by housing. Nondeprived rats (G) preferred the 5% solution (78.4% of their total ETOH intake, cp. Table 3) In contrast, socially deprived rats (LI and C) preferred the 20% solution. They took only 33 9% and 37 4% of their total ETOH intake from the 5% solution. Each housing condition caused a typical pattern of ethanol intake which developed after an initial period of 5–10 days and then remained relatively stable all over the 14-week period. During each week's one-day period of short-term isolation, the G rats consumed significantly, $t(25) = 5.7$, $p<0.001$, more ETOH than before and afterwards. In the first seven weeks the increase of ETOH intake was particularly high (+57.8%), then it declined during the following seven weeks but still a significant increase [+21.6%, $t(11) = 2.6$, $p<0.05$, was maintained]

*Ethanol Choice After Changes of Housing Conditions (Second and Third Section: Week 15–28 and 29–42)*

During section 2 and 3 the previous housing conditions were rotated Group-housed rats moved to contact cages, contact-caged animals to individual caging and isolated rats were put together in groups. In two of the three cases (G→C, C→LI) the housing change caused an increase of social deprivation, whereas in the third case (LI→G) the deprivation was terminated.

The transition from a lower to a higher level of deprivation was always followed by an increase of ETOH consumption, whereas in the opposite case the intake was either constant or even decreasing (Table 2). The higher intake of alcohol after intensified deprivation resulted in two distinct effects: a transient increase lasting for 1–2 weeks and a slow persisting increase. The transient effect was strongest during transitions from C to LI (Fig. 1). After three weeks when ETOH choice was reduced again the new level of intake ranged above the former one. A slow but persisting increase was typical for transitions from G→C.

During the first section of the choice experiment (week 1–14) the general trend of ETOH intake was negative (Fig. 1), there was a significant decline of alcohol consumption, $t(12) = 6.1$, $p<0.001$. After the first change of housing conditions (second section) the mean daily consumption remained constant for the next 14 weeks. After the second move (third section, week 29–42) the trend was positive, the rats took more ETOH from week to week, $t(12) = 3.4$, $p<0.01$ (Fig. 1). Independently from the actual housing condition the mean alcohol consumption was generally increasing from section to section (Table 1)

The concentration preferences during the sections 2 and 3 were only to a minor degree depending on the actual housing situation, but the former preferences developed during section 1 were largely maintained (Table 3) Short-term isolation (24 h) of rats usually housed in groups enhanced ETOH consumption again, $t(25) = 4.7$ and $t(25) = 4.4$, respectively, $p<0$ 01, respectively. Although during the sections 2 and 3 other animals than in section 1 were concerned, the quantitative level of the increase was nearly the same as during the last seven weeks of the first section (+20.7% in section 2, +23.4% in section 3).

*Diazepam Choice (Week 57–70)*

During this time period rats of both main experimental series (42 weeks of ETOH experience and naives) obtained D solutions and tap water. Control animals had the choice between tap water and all the constituents of the D-containing solution except from diazepam. During the first two weeks both experienced and naive rats preferred the diazepam solutions (60% of their total fluid intake). An even higher preference (85%) was found in the control rats suggesting that this initial effect was not specific for diazepam but for the additive constituents. After two weeks the intake behavior revealed increasing differences between test groups and controls. The latter maintained the high preference, whereas both experienced and naive test groups reduced their diazepam intake and then maintained a residual level of consumption until the end of the 14 weeks lasting phase (Figs. 2, 3a).

Diazepam taking was not affected by experiences with alco-

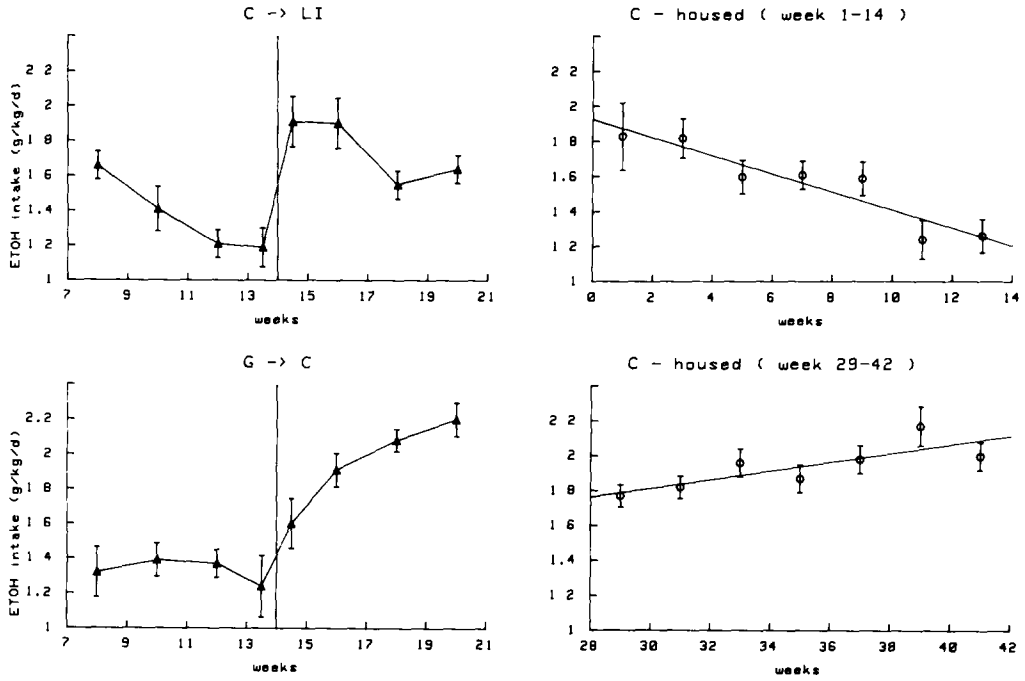


FIG 1. (left side) Mean ETOH intake (±SEM) before and after the first move to new housing conditions (vertical line) with an increasing degree of social deprivation Above C→LI Below G→C (right side) Mean ETOH intake (±SEM) of contact-housed rats Above first section of ETOH choice Below third section after two changes of housing (LI→G, G→C) Regression lines indicate temporal trends

hol· there were no significant differences between experienced (2.14 mg/kg/day) and naive rats (2.27 mg/kg/day). The time courses of intake were similar (Fig. 3a). ANOVA statistics revealed no significant differences between the housing groups neither in naive nor in experienced animals (cf. Table 2). Since the housing conditions had already been changed twice, this result does not disprove any relationship between D intake and social housing. Although previous ETOH experiences did not affect the attitude towards D, the hypothesis was to be tested that the indi-

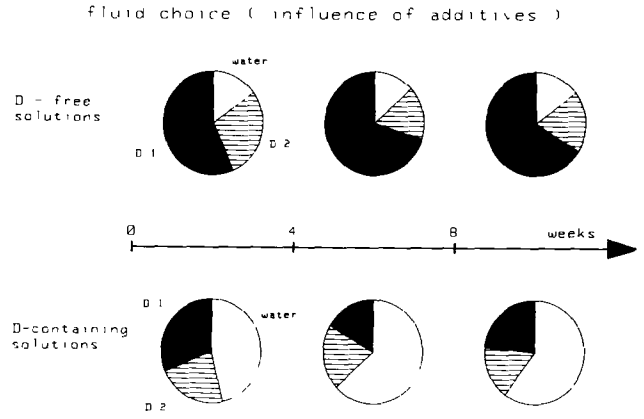


FIG 2. Pie charts for the preferences of fluid choice Mean volume portions for 1st–4th, 5th–8th, and subsequent weeks Above controls choosing between water and D-free solutions of additives (see the Method section) Below rats of the main series choosing between water and D-containing solutions (D/1 = 100 mg/l, D/2 = 50 mg/l)

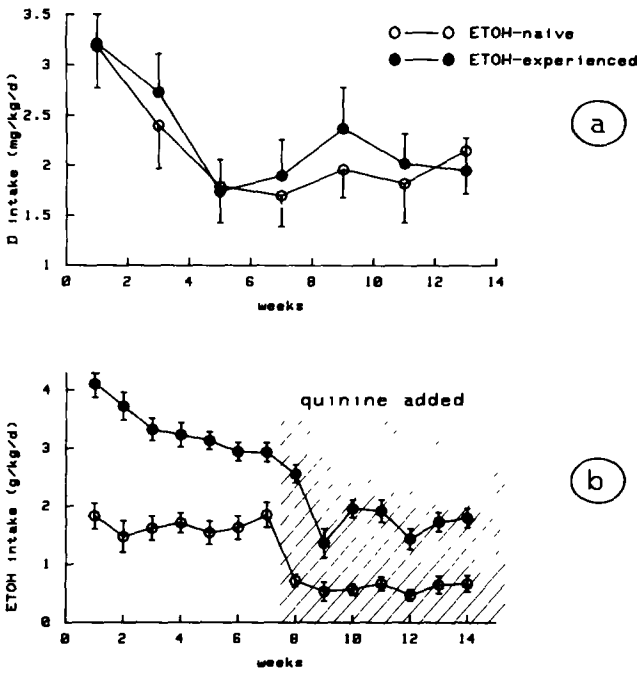


FIG 3. Consumption of D and ETOH by ETOH-experienced and ETOH-naive rats. (a) Mean time course of D intake (b) Mean time course of ETOH intake (±SEM, each) during the retest period. The ETOH choice succeeded to a 3-month drug-free period (in experienced rats 9 months without ETOH) Shadowed area increasing concentrations of quinine were added to the ETOH solutions

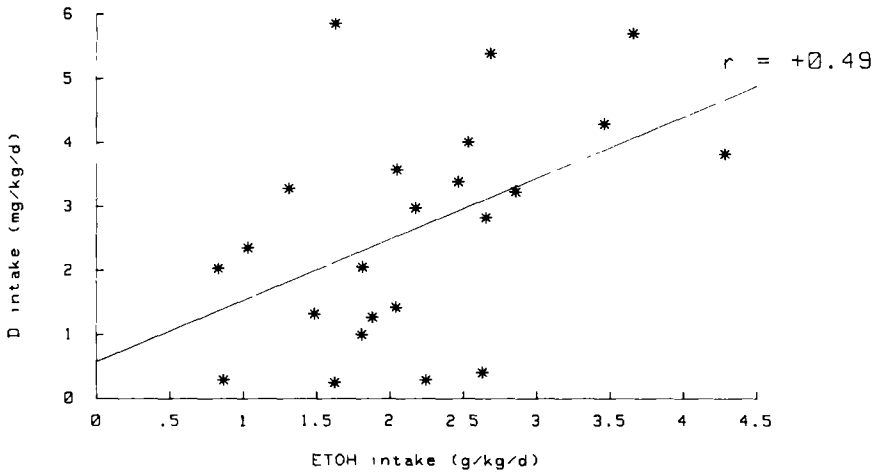


FIG 4 Correlation diagram and resulting regression line for the relationship between the mean ETOH intake (3rd section) and the mean D consumption of ETOH-experienced rats

vidual values of ETOH intake and D consumption correlated to each other. By this way a significant positive correlation between ethanol and diazepam intake was established ($r = +.5$, $p<0.02$; Fig. 4).

*Ethanol Reoffered*

A possible explanation of the independence of D choice from previous experiences with ETOH might be that during the first drug-free period the elevated preference for ETOH in experienced rats did not persist. To test this hypothesis all the rats (experienced and ETOH-naives) received ETOH solutions again after a second drug-free period. In contrast to the prediction (no differences), experienced rats consumed more than twice as much ETOH than naive ones, $t(29)=3.9$, $p<0.001$ (Fig. 3b). Experienced rats started at a high level of ethanol ingestion (4.18 g/kg/day); during the subsequent weeks the intake was gradually reduced. Naive animals maintained a low level of intake (1.7 g/kg/day) during the whole course of the choice period (Fig. 3b). In experienced rats the influence of housing conditions corresponded to that before the ETOH-free period but ETOH consumption was much higher than before (Table 2). The difference between experienced and naive rats was highly significant, $t(29)=6.2$, $p<0.001$.

During the following 7 weeks quinine was added to the ETOH solutions but not to tap water. The concentration was raised stepwise from week to week. Control rats revealed a strong aversion against all quinine concentrations: they drank less than 2% of the quinine solution. In another control experiment rats having experienced adulterated and nonadulterated ETOH solutions received both quinine-containing and noncontaining ETOH solutions apart from tap water. Although the animals were conditioned during the preceding four weeks to drink quinine-containing alcohol solutions they took ETOH preferably (74%) from the quinine-free solutions.

The previously ETOH naive animals reduced ETOH intake when quinine was added (from 1.67 g/kg/day to 0.61 g/kg/day, Fig. 3b). Experienced rats also reduced their ethanol intake, but

TABLE 4

DEVELOPMENT OF BODY WEIGHT, FOOD CONSUMPTION, AND FLUID INTAKE DURING THE COURSE OF THE EXPERIMENT (cf TABLE 1)

| | Body Weight (g) | | Food Consumption (g) | | Total Fluid Intake (ml) | |
|---|---|---|---|---|---|---|
| | Exp | Naive | Exp | Naive | Exp | Naive |
| Begin of 1st section | 282 4 ± 3 5 | 296 6 ± 7.0 | 24 1 ± 0.6 | 24 8 ± 0.6 | 33 9 ± 1.1 | 32 7 ± 1 7 |
| End of 3rd section | 470 4 ± 9 5 | 493 8 ± 13 9 | 24 4 ± 0 9 | 28 3 ± 1 4 | 35 6 ± 1 3 | 35 0 ± 2 0 |
| End of D choice | 493 6 ± 7 0 | 544 0 ± 17 1 | 23 4 ± 0 6 | 26.0 ± 1 6 | 32 0 ± 1.2 | 33 4 ± 1 3 |
| End of the experiment | 474 1 ± 13.9 | 520 0 ± 16 5 | 23 6 ± 0 6 | 27 5 ± 0 9 | 41 6 ± 2 9 | 36 8 ± 1 7 |

Mean values ± SEM for rats of the main series
exp = ETOH-experienced, naive = ETOH-naive

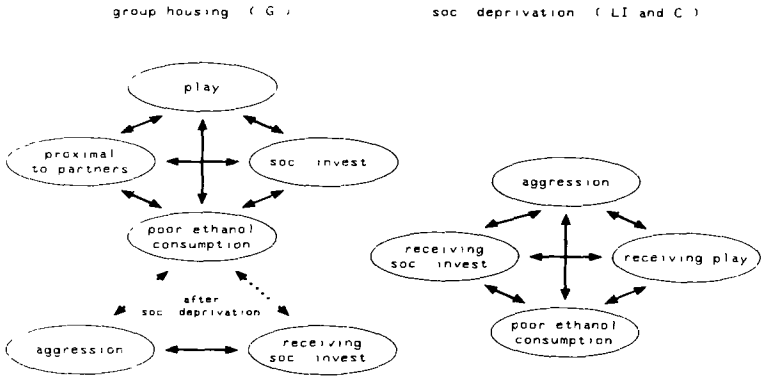


FIG 5 Significant ($p<0.05$) correlative relationships between behavioral features and ETOH consumption (right side) Initially deprived rats. The relationships to the features of dominance are maintained after the change of housing conditions (left side) Initially group-housed rats (individual ETOH consumption was measured during the periods of short-term isolation) After stable social deprivation new correlations to dominance appear (dotted arrows)

even with the highest quinine concentration they consumed more ethanol than naive rats drank from the nonadulterated solutions. Two exceptions from these rules were found· one experienced individual nearly ceased to take ETOH solutions (3.64 g/kg/day to 0.49 g/kg/day), whereas the addition of quinine (1.48 g/kg/day to 1.21 g/kg/day) did not show any effect in one of the naive rats.

Before the addition of quinine the preferences for ethanol concentrations depended on experiences and housing. On an average 36.7% (experienced) and 78% (naive) of the ETOH ingestion derived from an intake of the 5%-solution. During the quinine phase all individuals which maintained ethanol consumption switched their preference towards the 20%- solution and reduced their 5% intake (Table 3). By this means the quantity of quinine to be taken together with ethanol was minimised. For all the group-housed rats of the main series, the short-term isolation was continued once a week until the end of the experiment. ETOH-naive individuals revealed a similar increase of ETOH consumption [+15.2%; $t(12)=3.0$, $p<0.05$] as the experienced rats had shown during the last phases of ETOH choice. Alcohol ingestion of the latter rats, however, was no longer significantly affected by short-term separation from the other group members (+3 1%).

Apart from their different attitudes towards ETOH the individuals of the main series revealed no further discrepancies. Throughout the experiment, body weight, food consumption, and total fluid intake developed synchronously (Table 4). Prior to their first drug experiences, the experienced rats were already less heavy than their naive conspecifics. The weight ratio was nearly maintained over the experiments' two-year period

*Sets of Behavioral Features and Drug Choice*

To study possible interactions between drug taking and social behavior tetradic encounters were performed before first drug exposition. The analysis of the social behavior of an individual attempted to establish individual behavioral features and to detect sets of positively or negatively correlating features. G individuals differed from LI and C. For socially deprived animals (C and LI) two sets were established. The first one included features concerning the social activity of an individual (play, social investigation and spatial proximity to conspecifics); the second one comprised aggression and social recipience, it corresponded to the dominance rank [Fig. 5; (48)]. Group-housed rats (G) revealed three sets of features which reflected social activity, dominance rank (less pronounced than in LI and C), and exploration (time spent in the center of the arena, spatial distance to other rats, rearing, object targetting). The differences between the corresponding sets of deprived and nondeprived rats concerned the recipience of aggression by others. In LI and C aggressive acts were mostly directed to socially active animals, in G to low-ranking rats. The body weight of an individual was not correlating significantly to any of the behavioral features.

The evaluations aimed to identify behavioral features which were suitable to predict later ETOH consumption. For this purpose, mean ethanol intake of each individual during section 1 was treated like a behavioral feature and correlated to the other features. Indeed, the consumption parameter turned out to be incorporated in the sets of features described in the last paragraph. Again, differences between the housing groups were found. Socially deprived rats revealed significant, negative correlations between ethanol consumption and the features characterizing dominance rank, $r(14)<-63$, $p<0.01$ (Fig. 5), whereas the intake did not correlate to the feature set of social activity In normally group-housed rats which were isolated for one day significant negative correlations to the features of social activity appeared, $r(6)<-.84$, $p<0.01$ (Fig. 5). When the housing conditions were altered the individual attitudes of G rats towards ETOH were modified. As a consequence the relation to the "activity" features was attenuated and a new correlation to the dominance features developed (Fig. 5). In neither group ETOH consumption depended on the body weights.

The quantitative consequences of the correlative relationship were even more prominent than in the case of different housing. Dominant LI rats consumed only 43% of the quantity of ethanol that was taken by nondominant individuals (in C: 61%; Fig. 6). Socially active G rats consumed during phase 2 an average of 26.5% less ETOH than nonactive individuals, but such difference did not develop before the second week of exposition (Fig. 6). The negative correlation between alcohol intake and dominance rank was only found in stable social conditions (LI and C) When housing was changed dominant rats responded more sensitively than nondominant individuals and increased their consumption to a considerable degree (Fig 7).

When ETOH was reoffered after 18 months, the influence of social dominance on ETOH choice was initially present but disappeared after four weeks. In the following ten weeks (including the quinine phase) no significant differences between dominant and nondominant rats could be detected (Fig. 8).

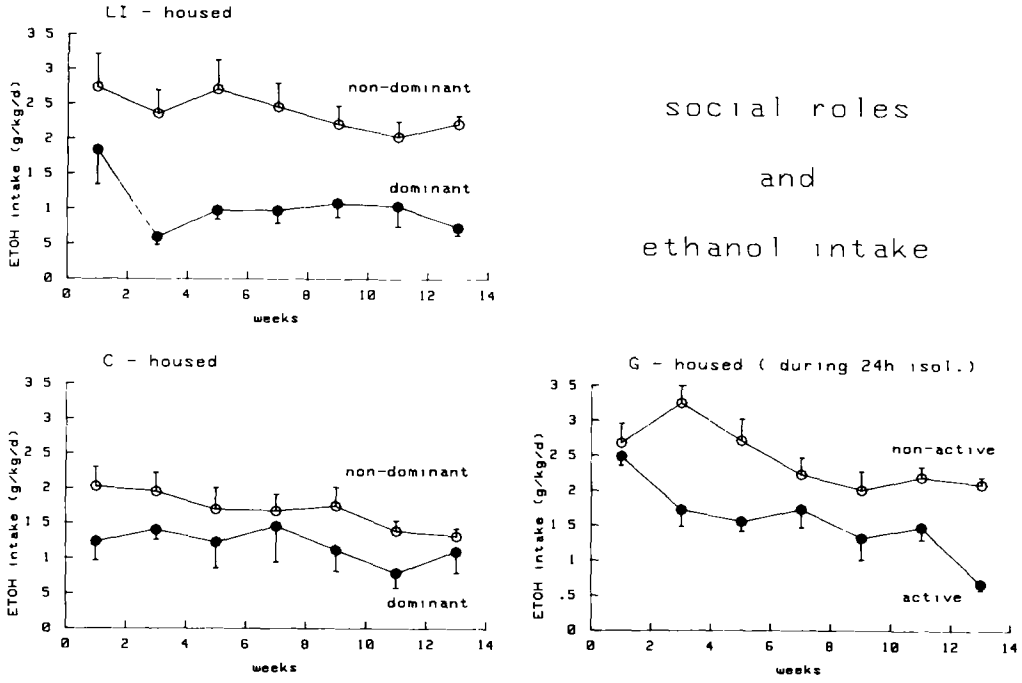


FIG 6 Mean time course of ETOH intake (±SEM) depending on the rats' social roles In socially deprived animals (LI and C) dominant and nondominant rats are discriminated, in G social activity determines the ETOH consumption

In the same way as for ETOH, the individual rank numbers of D intake doses were correlated to the behavioral features In socially deprived rats (LI and C), the results corresponded completely to those obtained for ETOH. The intake feature was connected to the cluster of social dominance and revealed significantly negative correlations, $r(34) < -53$, $p < 0.001$, to aggression and recipience of social behavior In G-housed rats, however, the pattern was similar as in LI and C. Diazepam consumption was also incorporated into the cluster of dominance (cf. Fig. 5). Neither social activity nor body weight correlated significantly to the drug choice of any housing group

The differences between the doses of diazepam taken daily by dominant and nondominant rats were considerably high and, on average, even more pronounced than for ethanol consumption From the beginning of D exposition nondominant individuals consumed 38% more of the drug, after the general decrease of D intake (4–6 weeks) dominant rats maintained a low level of consumption, whereas the D preference of nondominant individuals recovered, $t(31) = 3.1$, $p < 0.01$ (Fig. 9).

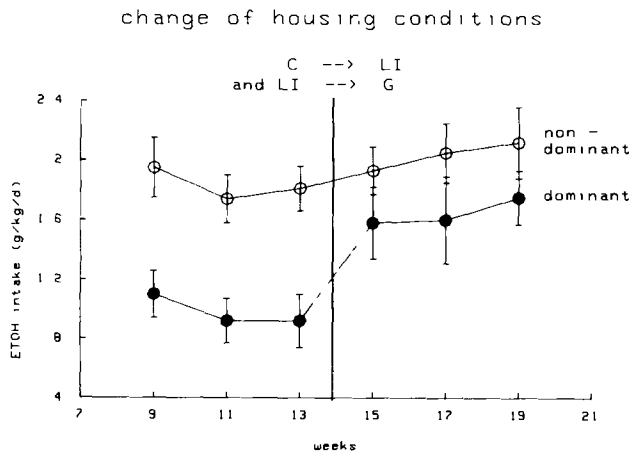


FIG 7 Mean time courses of ETOH intake (±SEM) by dominant and nondominant rats before and after a change of housing conditions The rats were moved from a stable social condition (LI or C) to a new social environment (G or LI) Social deprivation was either increased or suspended

## DISCUSSION

### *Environmental Factors*

Previous experiments have shown that environmental factors, in particular social conditions, influence the voluntary intake of ETOH by rodents and primates (2, 7, 10, 13, 21, 22, 24, 45). Apart from the daily dose taken by the animal the preferences for certain concentrations and the circadian pattern of consumption were affected [(10,45), cf. (39)] The present results confirm that both short-term and long-term social isolation enhance the consumption of ETOH, especially of highly concentrated solutions. Since contact-caged rats revealed a reduced preference for alcohol it may be concluded that the effect of isolation is due to sensory deprivation rather than to the disability to perform playful and agonistic behavior (45,46). The differential intake of ETOH by rats kept in different social environments suggests that the psychotropic effects of alcohol or its metabolites rather then olfactory and gustatory stimuli are mediating drug-taking behavior. An experienced individual takes that quantity and that concentration of the drug which is best suitable to elicit the desired psychotropic effects [(2, 7, 13, 45), cf. (32)].

When a rat is kept in constant circumstances it develops a

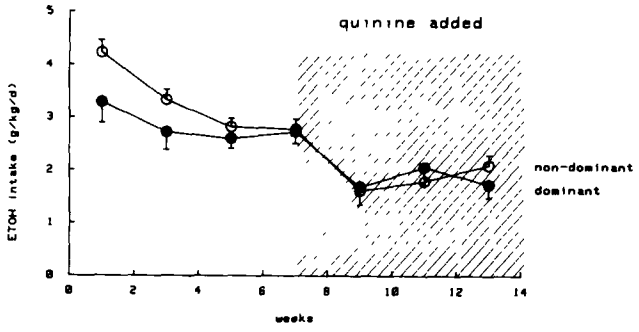


FIG 8 Influence of social dominance on ETOH choice in experienced rats when ETOH is reoffered after a long drug-free period Mean time courses of ETOH intake (±SEM, ETOH-retest) Hatched area quinine added

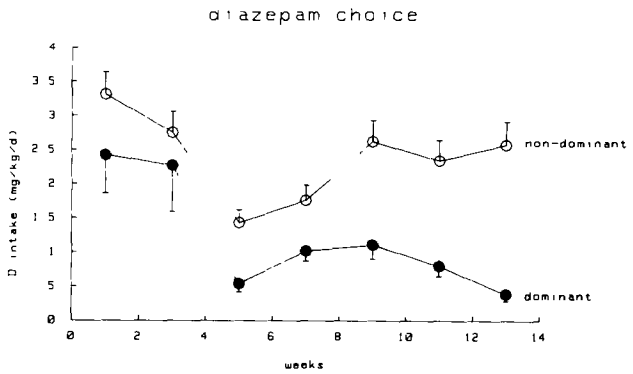


FIG 9 Mean time courses of D intake (±SEM) by dominant and non-dominant rats

stable pattern of ETOH consumption (45). An abrupt change of the housing condition not only leads to a new social situation to which the rat has to adapt but also acts as a potent stressor. The dramatic rise of ETOH drinking during short-term isolation which partially habituates after several weeks might be due to such an effect of isolation distress (45). An alternative explanation is that the increase reflects the adaptation of alcohol consumption to the new requirements. Similar effects of adaptation and/or transient stress are observed when the rats are moved from one housing condition to another. An enhancement of social deprivation always causes an increase of consumption. When contact caging is followed by single housing the persistent increase is superimposed by a transient "overshoot" of ETOH consumption With the present results it cannot be decided whether this is a response to stress or an adaptive learning how to take the drug in the new situation.

On the other hand, a gain of social contacts was expected to diminish the intake of ETOH markedly. However, the decrease of consumption was much weaker than the increase caused by a comparably enhanced deprivation It may be concluded that the social situation not only comprises actual and reversible effects but also gives rise to persisting alterations (12).

*Individual Factors*

In outbred strains of rats the interindividual variation of voluntary ETOH intake is rather high (13, 37, 38, 45) Such a variability may reflect individual factors affecting the behavior of the animal towards the drug. In the present study we tried to characterize the behavior of each rat individually before the beginning of the drug taking experiment If it would be possible to discriminate between different "types" of individuals such classification might offer a prediction for drug taking later on. "Tetradic" encounters in the open field (46) are suitable to characterize the social and nonsocial behavior of an individual (48) With a high degree of reliability individual behavioral features can be established which comprise the rat's own behavior as well as its social recipience [i.e , the behavior of the other animals towards it, (48)]

Assuming that a rat can be attributed to a ' social role" a certain set of features would be expected to characterize this role. In the behavioral recordings of this study two sets of features were identified which indicated two different roles· social dominance and social activity. Dominant individuals were more aggressive than others (including aggressive acts and postures occurring during play) and received more social interactions by others, whereas active rats initiated sequences of social contact and play.

Social dominance revealed a significant, negative correlation to the consumption of ETOH and D. The quantitative effects were even stronger than those of the housing conditions. On the average, nondominant rats took more than twice as much of the drug than dominant ones did The dominance rank of a rat individual is stable over long time periods (3) This corresponds to our results that the correlation was still present after more than one year. A similar relationship between social dominance and alcohol consumption has been pointed out by other authors who have assumed that the enhanced drug intake by low-ranking individuals might be caused by stressors deriving from social competition (2,13) The results of the present study are not in accordance with this hypothesis. The negative correlation between dominance rank and drug preference was most prominent in those individuals which were separated from each other for long time periods. Neither during nor shortly before ETOH choice was social stress present. Instead, the data suggest a common individual disposition for the intake of ETOH and D correlating to dominance rank. Such a disposition may be related to differentiated responses to the drug by dominant and nondominant individuals which depend on hormonal factors and neuronal adaptations [(11, 30, 40), cf. (20)].

Only in one case no negative correlation between drug consumption and dominance rank was found. This exception concerned the G-housed rats which were kept in groups but isolated for 24 h once a week. In this housing situation the socially active rats were the least consumers. There are indications that not group-housing itself but the intermittent changes of environmental conditions are responsible for the diverging result With rats which were moved once a week from one housing condition to the next we found no correlation between alcohol preference and dominance (Heyne and Wolffgramm, in preparation). In the present study a change of housing conditions raised the intake of ETOH, especially in dominant rats These results suggest that under stable circumstances dominant rats are poor drug users, but they seem to be more sensitive to social instabilities

*Temporal Development*

The long duration of the experiment enabled a discrimination between different phases of voluntary ETOH consumption. During the first 1–2 weeks drug-naive rats took high daily doses of the drug which varied from day to day. A stable individual pat-

tern of consumption did not develop before the second or third week of access to ETOH (45). It is likely that in this time the animals experienced the drug effects (7). During the subsequent six months drug taking behavior remained relatively stable, each rat established an individual pattern of consumption which was modified by environmental factors in a predictable way. After this time the mean consumption of alcohol continued to rise independent of the social condition. Such an increase may be due to the development of an unconditioned or conditioned drug tolerance (18), but it might also reflect an increasing demand of the rat for stronger effects [cf. (37)].

After several months without access to ETOH the intake of alcohol by experienced rats differed distinctly from that of ETOH-naive individuals. It was characterized by a raised level of drug consumption which was maintained even when a taste-aversive constituent [quinine; (1,17)] was added to the ETOH solutions. Such a behavior reveals remarkable similarities to "psychic dependence" of humans on alcohol (4, 7, 28, 29) In both cases a high preference for the drug is perpetuated through long drug-free periods and the reward caused by the intake of ETOH can hardly be antagonized by aversive stimuli. Since it was not possible to assess emotional variable in the rat, it seems adequate to characterize the rat's behavior as "behavioral dependence" (25) During this period interfering social factors lose their influence Housing conditions, individual behavioral features like dominance and social activity, and isolation distress were no longer significantly affecting ETOH consumption. Thus, social factors serve as triggers for the development of behavioral dependence but when this state is reached, they no longer affect it (7). The rigorous demand for the drug which is not extended over long periods and the decreasing influence of modifying factors is comparable to the "loss of control" in human alcoholics (4, 7, 29)

The development of behavioral dependence on ETOH did not affect the voluntary intake of D. Both the daily doses and the time courses of consumption were the same in ETOH-naive and experienced rats. Thus, the rewarding properties of ETOH could not be substituted by D. There was no behavioral cross-dependence, although both compounds have in part a similar spectrum of actions and even cross-tolerance and physical cross-dependence between ETOH and benzodiazepines have been reported (5,6). The drug specificity of behavioral dependence contrasts with the individual disposition for drug intake mentioned before which affects ETOH and D in a similar way. Thus, drug-specific as well as drug-unspecific mechanisms contribute to the development of drug dependence.

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