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Effects of Ethanol on Behaviour of Aggressive Mice from Two Different Strains: A Comparison of Simple and Complex Behavioural Assessments

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SMOOTHY, R. AND M. S. BERRY. *Effects of ethanol on behaviour of aggressive mice from two different strains: A comparison of simple and complex behavioural assessments.* PHARMACOL BIOCHEM BEHAV 19(4) 645–653, 1983.—The effects of acutely administered ethanol (0, 0.5, 1.0 and 2.0 g/kg IP) were studied in two strains of aggressively-rated, individually-housed male mice in encounters with non-drugged "standard opponents." Behaviour was quantified using both a complex ethological analysis of frequency of occurrence of acts and postures, and a more simplified analysis of time spent in 4 broad behavioural categories (non-social, social/sexual, aggressive and timid/defensive). The simplified analysis failed to reveal certain trends that were detected by the more complex analysis. The principal effects of alcohol on behaviour were a dose-dependent suppression of aggressive activities (with no evidence of a biphasic effect), an increase in timid/defensive behaviours, and changes in many non-social and social/sexual acts and postures. There were no qualitative inter-strain differences, but Swiss mice were markedly more sensitive to the drug than TO mice, particularly in their non-social, aggressive and timid-defensive behaviours. Strain differences in blood alcohol levels were only apparent at the lowest dose.

Ethanol Mice Social interactions Ethological analysis Blood alcohol levels Strain differences Agonistic behaviour

ALCOHOL influences many aspects of social behaviour in a variety of vertebrates, including fish [18], birds [22], rodents (see below), cats [25], dogs [30] and monkeys [14]. Much of this work has concentrated on the relationship between alcohol and aggressive behaviour, possibly because of the presumed link between human violence and alcohol intake [12,17].

Animal models to study the effects of alcohol on aggression have commonly employed rats and mice in a variety of behavioural situations. High doses of alcohol have consistently been shown to suppress aggression in both species, while lower doses have potentiated this activity in some studies, but suppressed or left it unchanged in others. Potentiation of aggression has been shown, for example, by Miczek and O'Donnell [27], who found that 0.3 g/kg ethanol increased both attack and sideways threat in Swiss mice tested in neutral cages, but not in their home cages. They concluded that low doses of alcohol facilitated the expression of suppressed aggression. There was an apparent biphasic effect of alcohol, since sideways threat was significantly decreased by a dose of 1.2 g/kg. Kršiak [23] found that some aspects of aggressive behaviour were increased in aggressive, isolated mice at a dose of 0.4 g/kg, but were suppressed at higher doses (0.8 to 2.4 g/kg), also suggesting a biphasic effect. This latter study revealed a potentiation of aggression in timid, isolated mice at 0.8 g/kg, but no significant change at the other doses tested, suggesting that the observed drug effects are dependent on the nature of the recipient. Similar conclusions were reached by Miczek and Barry [26] using dominant, subordinate and naive rats.

Some rodent studies however, have failed to show a potentiation of aggression with low doses of alcohol, for example in a tube-restraint/shock-induced model in rats [33] and in inter-male aggression in mice [5]. Previous work on isolated mice in this laboratory also showed that doses as low as 0.1 g/kg suppressed rather than potentiated aggressive behaviour [32].

The studies cited above used a variety of species and strains in a wide range of situations which perhaps measure diverse forms of aggression (see Brain [7] for a discussion of the problems of extrapolating between different "models"). These differences in methodology may help to account for the variance in results on aggressive responding.

There are also wide differences in the methods used to

analyse behaviour. Some of the above studies [23, 26, 27, 32] measured frequencies and/or durations of both aggressive and non-aggressive acts and postures in the same trial; this provides useful information about the influence of alcohol on non-aggressive behaviours, and in addition gives an indication of the specificity of its effects on aggression. Many studies however, have not used such detailed behavioural inventories for assessing the effects of alcohol, but have concentrated on single measures such as squealing frequency [5], target-biting frequency [33], and the percentage of electric shocks producing fighting behaviour [35]. These latter methods have the advantage of simplicity, but more detailed, ethological analyses have been strongly advocated [21, 24, 28, 31] because they seem to provide a much more precise profile of drug action. In the present study, ethological techniques have been applied to assess the influences of alcohol on social behaviour in mice; 2 different levels of complexity of analysis have been used, to determine whether they both provide similar profiles of drug action on behaviour, and to assess their respective sensitivities in detecting drug-induced changes in behaviour. Measurements were made of the frequencies of 61 behavioural acts and postures (both aggressive and non-aggressive), and also (more simply) time spent in 4 broad categories of behaviour (namely non-social, social/sexual, aggressive and timid/defensive activities).

The analyses were carried out on individually-housed mice injected with either 0, 0.5, 1.0 or 2.0 g/kg ethanol, encompassing the dose range reported in previous studies to both increase (low dose) and decrease levels of aggression. Mice were isolated for 2 weeks and then tested for aggressiveness in a non-drug screening trial. Kršiak [23] has shown that aggression is not always shown by isolated animals, and isolates could be rated as either aggressive, sociable or timid. In the present study, similar categories of isolates were distinguished, but only aggressive individuals were subsequently used. Since different types of isolate respond differently to alcohol [23], this pre-selection ensures more uniform behavioural levels within the test sample. Effects of alcohol on sociable isolates will be treated in a subsequent publication (Smoothy and Berry, in preparation). Two outbred strains of mice were studied to provide information on genotypic influences on alcohol and social behaviour.

METHOD

Subjects

Male Swiss-Webster and Tuck "TO" strain mice were used in these experiments. Both strains had been bred for many generations in the Animal Facility at the University College of Swansea, but were originally obtained from Schofield and Co., Lancs., and A. Tuck and Sons Ltd., Essex, U.K., respectively. Mice were weaned at 19–23 days of age and housed in single-sex groups of 6 animals in opaque plastic cages, 30×12×11 cm (North Kent Plastics, U.K.). Sawdust substrate was regularly replaced, and apart from experimental manipulations, this was the only time subjects were disturbed. Animals were maintained under highly controlled conditions of temperature (18–22°C), with a reversed light cycle (fluorescent lights on from 22.30 until 10.30 hours). Food (Pilsbury's Small Animal Diet) and water were available ad lib, except during behavioural trials. Animals were between 55 and 65 days of age when tested (Al-Maliki [3] has shown that intraspecific isolation-induced fighting occurs as early as 35–36 days of age, and no significant differences are observed in aggression levels between the ages of 35 to 100 days of age).

Seventy-five randomly selected male Swiss mice and 130 male TO mice were individually-housed in standard cages for 16 days before drug testing. This "isolation" procedure increases the likelihood of recording aggression in encounters between male mice [19,34]. In addition to aggressivity, individually-housed mice differ from group-housed counterparts with respect to many other behaviours, such as activity and ambulation in a novel arena [9]. There is much evidence however, that these changes are not brought about by isolation "stress"—individual-housing appears no more stressful to mice than group-housing [6].

An additional 205 male Swiss mice were kept in groups of 6 after weaning, to be used as "standard opponents" [8]. "Standard opponents" are docile male animals that will elicit attack behaviour from aggressive partners, but never themselves initiate attacks or show signs of overt aggression [3,10]; any fighting is consequently unidirectional and assumed to reflect the experimental manipulation of the test animal [29]. In the present study, "standard opponents" were group-housed males rendered anosmic by the application of approximately 25 μl of 4% zinc sulphate solution to the nasal tract under ether anaesthesia [2,4], both 3 days and 1 day prior to encounters—such opponents were never used more than twice or at intervals of less than 5 days. Peripherally-induced anosmia is not thought to interrupt non-sensory functions of the olfactory organ system [29], and therefore does not produce disturbances in behaviour unrelated to anosmia (which may be caused by centrally-induced anosmia by olfactory bulbectomy [1]). The advantages of using such "standard opponents" have been fully discussed by Brain *et al.* [10].

Screening Trials

On the 14th day of isolation (48 hours prior to the drug trial) all subjects were tested with a "standard opponent" to establish whether the isolate was aggressive or non-aggressive. The Swiss "standard opponent" was marked with methyl violet fur-dye and introduced into the home cage of the test animal for 500 seconds. Neither isolates nor intruders received injections in these trials.

Aggressive isolates were defined as those animals that showed at least 10 seconds of aggressive behaviour and/or at least one biting attack during this trial. An additional prerequisite was the absence of timid/defensive behaviour, defined arbitrarily as the mouse showing less than 10 seconds of such behaviour during the encounter.

Drug Trials

Forty Swiss and 48 TO mice rated as aggressive were subsequently obtained for the drug trials, which took place 48 hours after screening trials. Twenty minutes prior to testing, subjects were injected IP with either 0.9% saline (control animals) or one of 3 doses of 99.6% ethanol diluted in saline (0.5, 1.0 or 2.0 g/kg body weight). Different drug doses were administered by varying the concentration while keeping the injected volume constant at 0.1 ml per 10 g body weight. Each subject received only one injection and one drug trial. Tests commenced 1 hour after the onset of the dark phase of the illumination cycle and continued for a maximum of 2.5 hours in order to minimise effects of circadian fluctuations in aggressive behaviour [36].

Twenty minutes after injection, a randomly chosen (non-

injected) "standard opponent" was placed in the subject's home cage for 500 seconds. Each encounter was video-taped from vertically above the testing arena under conditions of dim red lighting, using a low-light video camera (National Panasonic: WV 260) and video recorder (JVC: CR 6060 E) with a superimposed time trace (For-A Limited). Recording was facilitated by removing the cage lid one minute before the introduction of the "standard opponent" and replacing it with a transparent perspex cover.

The following behavioural measures were ultimately obtained from analysis of video tapes. (1) Latency to attack the intruder. (2) Total time allocated by subjects to the categories of (a) non-social behaviour, (b) social investigation/sexual behaviour, (c) aggressive behaviour and (d) timid/defensive behaviour [13,16]. These items were measured with a four-channel electronic timer used simultaneously with the playback of the video tape, and this constituted the more simplified type of analysis. (3) The frequencies of all the individual acts and postures shown by the subject (i.e., a more complex ethological analysis), aided by freeze-frame and frame-advance facilities on the video-recorder. These acts and postures were allocated to the 4 broad categories of behaviour used in section 2, and were based on the checklist published by Grant and Mackintosh [20].

Non-social postures. The elements "circle," "zig-zag," "figure-of-eight," "wash," "self-groom," "dig," "kick dig" and "push dig" were all as defined by Grant and Mackintosh [20]. The remaining non-social acts and postures were defined as follows: "scratch"—mouse uses hind limb to scratch its body; "explore"—mouse walks around the cage, direction of locomotion not apparently oriented towards opponent; "scan"—side to side movement of the head, attention not apparently concentrated upon opponent; "squat"—period of immobility with no overt signs of autonomic arousal; "rear"—front part of the body raised from the ground, no overt signs of autonomic arousal; "cage rear"—as in "rear," except fore paws rest against cage wall; "bounce"—mouse somersaults into the air; "leave"—mouse walks directly away from opponent; "abbreviated groom"—single rapid wipe of the head using the forepaws; "shake"—a brief, mild tremor of the body.

Social/sexual postures. The elements "approach," "investigate," "nose," "sniff," "stretched attention," "follow," "walk-around," "mount," "attempted mount," "post copulatory groom" and "crawl under" have all been previously described [20]. The remaining elements of this category were defined as follows: "push against"—mouse presses itself against opponent and the 2 animals squat together; "attend"—attention directed towards opponent, head parallel to mid-line of body; "head orient"—attention directed towards opponent, head at an angle to body; "box"—mice maintain mutual bipedal posture and push at each other with the forepaws; "opponent rear"—front part of the body raised from the ground while facing and in close proximity to the opponent, no overt signs of autonomic arousal; "groom"—mouse grooms body (excluding head region) of opponent; "push past"—mouse pushes itself between body of opponent and cage wall; "spin round"—mouse rapidly turns to face opponent; "crawl over"—mouse places both forepaws on opponent.

Aggressive postures. The acts and postures of "threat," "lunge," "attack," "chase," "aggressive groom," "upright offensive," "sideways offensive" and "tail rattle" were all as defined by Grant and Mackintosh [20]. An additional element, "charge," was defined as the mouse running rapidly towards the opponent.

Timid/defensive postures. The elements "flag," "evade," "flee," "crouch," "upright defensive," "sideways defensive," "upright submissive" and "full submissive posture" have been previously defined [20]. The remaining postures and acts allocated to this category of behaviour were defined as follows: "flinch"—rapid retraction of head and front part of body directly away from opponent; "retreat"—mouse runs away from approaching opponent; "startle"—sudden vertical leap in which all 4 feet leave the ground; "defensive posture"—similar to "squat" except that animal pushes itself against cage walls and body often showns quivering motions; "wall clutch"—mouse presses its ventral surface against cage wall, with forelimbs widely splayed.

Frequencies of occurrence for each act and posture on the above list were obtained for each drug dose group and the control group in both strains. Comparisons between groups were statistically analysed by the non-parametric Mann-Whitney "U" test [15].

Blood Ethanol Concentrations

Fifteen 60-day old mice of each strain from the same source as the animals used in behavioural encounters were used for determinations of blood ethanol concentrations. Blood (0.5 ml) was taken from the jugular vein under ether anesthesia, 20 minutes after injection of either 0.5, 1.0 or 2.0 g/kg doses of ethanol. Blood alcohol content was measured with a Boehringer Test-Combination kit, based on the conversion of NAD to NADH by enzymatic dehydrogenation of alcohol using alcohol dehydrogenase [11]. The NADH produced was measured spectrophotometrically (Pye Unicam SP 505, wavelengh 340 nm).

RESULTS

Screening Trials

In order to obtain the required number of aggressive mice of each strain, it proved necessary to give screening trials to 75 Swiss and 130 TO mice. Thus, while 53% of Swiss mice showed sufficient aggression after 14 days of individual housing, only 37% of TO mice showed this trait. The behavioural activity levels of the mice selected on the basis of the screening trials are given in Table 1. The Swiss subjects had higher baseline levels of aggression than corresponding TO mice, showing more attacks ($p<0.001$), longer durations of aggressive activities ($p<0.01$) and a shorter latency to attack ($p<0.001$). In addition, Swiss mice showed longer durations of non-social activities ($p<0.001$) and timid/defensive behaviour ($p<0.001$), whereas TO mice spent more time in social/sexual activities ($p<0.001$).

Drug Trials

Non-social activities. Time spent in non-social behaviour showed no significant changes at any alcohol dose in Swiss mice and a significant increase only at the highest dose in TO mice ($p<0.05$) (Fig. 1). Despite this finding however, the ethological analysis of acts and postures revealed many significant changes in both strains (Fig. 2), although the changes were not always the same in both strains: "explore," "scratch," "self-groom" and "shake" frequencies were all suppressed significantly at 1.0 and 2.0 g/kg doses of ethanol in Swiss mice, but were unchanged in TO mice. This was not

TABLE 1

MEAN VALUES FOR BEHAVIOURAL ACTIVITIES OF MICE RATED AS AGGRESSIVE IN SCREENING TRIALS

Strain	Latency to attack (sec)	Number of attacks	Duration of non-social activities (sec)	Duration of social/sexual activities (sec)	Duration of aggressive activities (sec)	Duration of timid-defensive activities (sec)
Swiss-Webster (n=40)	105.2	22.3	243.50	167.76	85.56	3.18
"TO" (n=48)	251.0†	15.4†	191.81†	245.80†	60.99*	1.40†

*$p<0.01$, significantly different to Swiss mice.
†$p<0.001$, significantly different to Swiss mice.

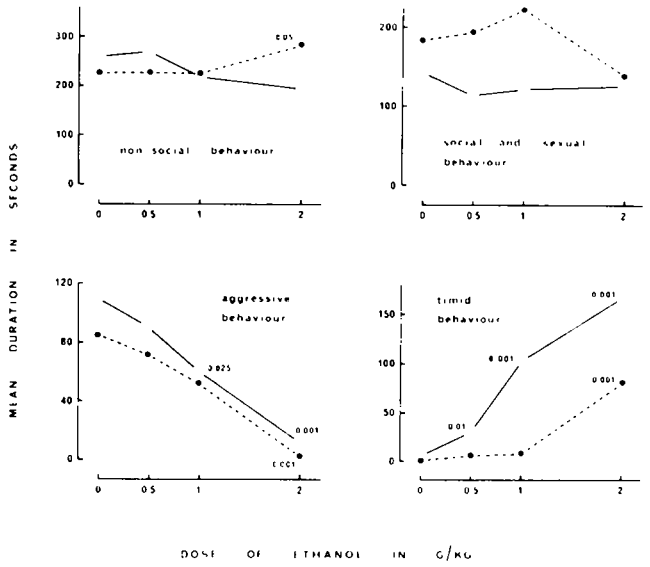

FIG. 1. Effect of ethanol on duration of 4 broad categories of behaviour of aggressive, singly-housed male mice during interactions with non-drugged "standard opponents." Open circles, Swiss mice; closed circles, TO mice.

necessarily due to differences in baselines (it is naturally easier to see a suppression of a particular behaviour if its initial level is high) because although it was higher in Swiss mice for "explore" and "shake," it was very similar for "scratch" and "self-groom." "Squat" showed a significant increase in frequency of occurrence at the highest dose in TO mice, but remained unchanged in Swiss mice.

Many acts and postures were changed by ethanol in both strains: "scan" frequency for example was increased while "leave," "cage rear," "rear," "abbreviated groom" and "dig" were suppressed in both Swiss and TO animals (Fig. 2). For most of these items however, significant behavioural changes were induced at 1.0 g/kg in Swiss mice, but only the highest dose was effective in TO counterparts. Indeed, in 10 of the 12 non-social elements which showed significant changes, such a change was seen at a lower dose in Swiss mice than in TO mice. TO mice only showed a significant behavioural change at an ethanol dose lower than in Swiss mice in "squat" frequency (this posture actually remained unchanged in Swiss animals).

The following postures showed no significant changes: "circle," "kick-dig," "push dig" and "bounce." The elements of "zig-zag" and "figure-of-eight" were not observed in any trial for either strain.

Social/sexual activities. Ethanol had no significant effect on time spent in social/sexual behaviour in either strain (Fig. 1). Although ethanol did not alter overall time allocated to such activities however, the postural analysis showed significant changes for particular elements (Fig. 3), some of which occurred exclusively in one strain. "Approach" and "post copulatory groom" were significantly suppressed by higher doses of ethanol in Swiss mice, but were unaffected in TO mice. "Sniff" and "groom" on the other hand were supressed by the highest ethanol dose in TO animals, but were unaffected in Swiss mice. Elements such as "walk-around" and "crawl over" were suppressed by ethanol in both strains. "Attend," "head orient," "investigate" and "nose" showed no significant response to ethanol in either strain. There appeared little evidence for a potentiation of any social/sexual act or posture in Swiss mice, apart from a dose-dependent increase in "stretched attention," which may be more characteristic of timidity than sociability. TO mice showed a significant increase in "stretched attention" at the highest dose of ethanol. They also showed increases in "follow" and "crawl under" at the 1.0 g/kg dose, but not at the highest dose.

Of the 9 behavioural elements showing significant changes, 4 of these occurred in lower doses in Swiss mice and 4 others at lower doses in TO mice. "Crawl over" was changed at the same dose in both strains. This shows a different pattern to the non-social postures, in which the Swiss mice almost invariably responded at lower doses than the TO mice.

No significant changes for either strain were seen for "push against," "box," "opponent rear," "head groom" "push past" and "spin round," but these were all characterised by very low baseline levels in the saline controls. "Mount" and "attempted mount" were not observed in any trial for either strain.

Aggressive activities. Analysis of time spent in aggres-

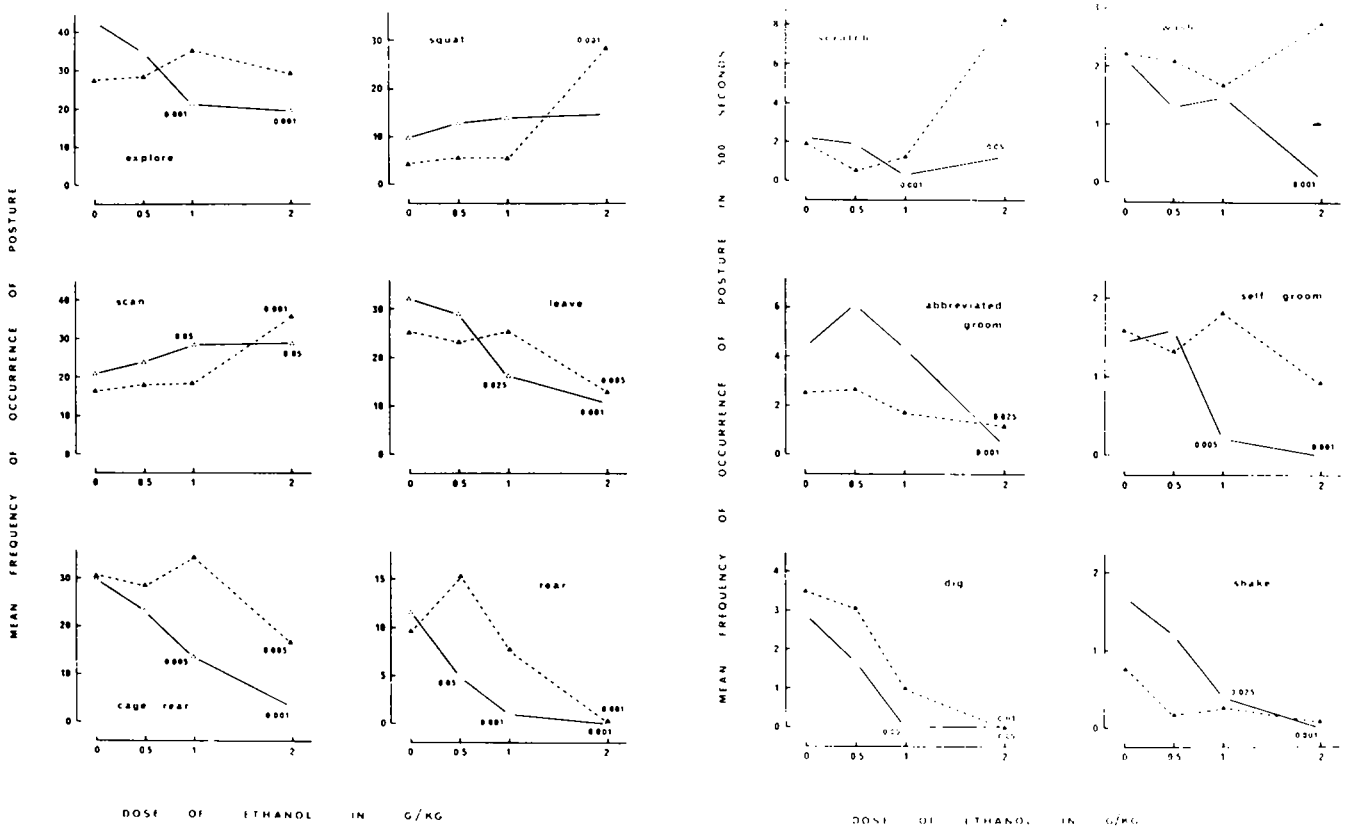

FIG. 2. Effect of ethanol on frequency of occurrence of various non-social acts and postures shown by singly-housed male mice during interactions with non-drugged "standard opponents." Open triangles, Swiss mice; closed triangles, TO mice.

sive behaviour showed significant decreases in duration of these activities at both 1.0 and 2.0 g/kg for Swiss mice, while TO mice only showed a significant suppression at 2.0 g/kg (Fig. 1). There was no evidence of the biphasic action of ethanol on aggression reported in some other studies.

In the ethological analysis of acts and postures, most aggressive elements showed the same pattern of dose-dependent suppression with increasing ethanol dose in both strains (Fig. 4). Decreases were observed in the elements of "threat," "lunge," "attack," "chase," "upright offensive," "sideways offensive," and "tail rattle." Certain elements, such as "attack" and "upright offensive" seemed to be particularly sensitive to the effects of alcohol; both were significantly suppressed by the lowest dose in Swiss mice and the intermediate dose in TO mice, but such suppressions were not detected by the simplified analysis. Significant effects of alcohol were observed at lower doses in Swiss mice in 6 out of the 7 postures that showed significant changes. Only "lunge" was decreased at the same dose in both strains. Swiss mice thus appeared to be more susceptible to the effects of alcohol on aggression than TO mice, although both strains showed the same patterns of responding, namely dose-dependent suppressions.

The latency to attack showed a dose-dependent increase with increasing ethanol dose, which was significant at 1.0 and 2.0 g/kg for both strains (Fig. 5)

The acts and postures that did not change significantly were "charge" and "aggressive groom," both characterised by low baseline levels in control animals.

Timid/defensive activities. Mean duration of time spent in timid/defensive behaviour showed dose-dependent increases in both strains (Fig. 1). Swiss mice showed significant potentiations at all 3 doses; in TO mice the increase was only significant at the highest dose.

The postural analysis showed dose-dependent increases in most timid/defensive acts and postures in both strains (Fig. 6). All these activities were elicited merely by the presence of a non-aggressive conspecific and were thus elements of "active" flight [23]. The elements of "flag," "flinch," "retreat," "upright defensive," "sideways defensive," "crouch" and "defensive posture" all increased significantly in both strains. However, in 7 out of the 9 postures which showed significant changes under the influence of alcohol, Swiss mice responded at doses lower than TO mice. Of these elements, "evade" and "flee" were changed significantly only in the Swiss strain. "Crouch" and "flinch" were changed significantly at the same dose in both strains.

The elements of "startle," "upright submissive," "full submissive posture" and "wall clutch" were not altered significantly at any dose tested.

Blood Alcohol Levels

Blood alcohol levels for both strains at 20 minutes post-

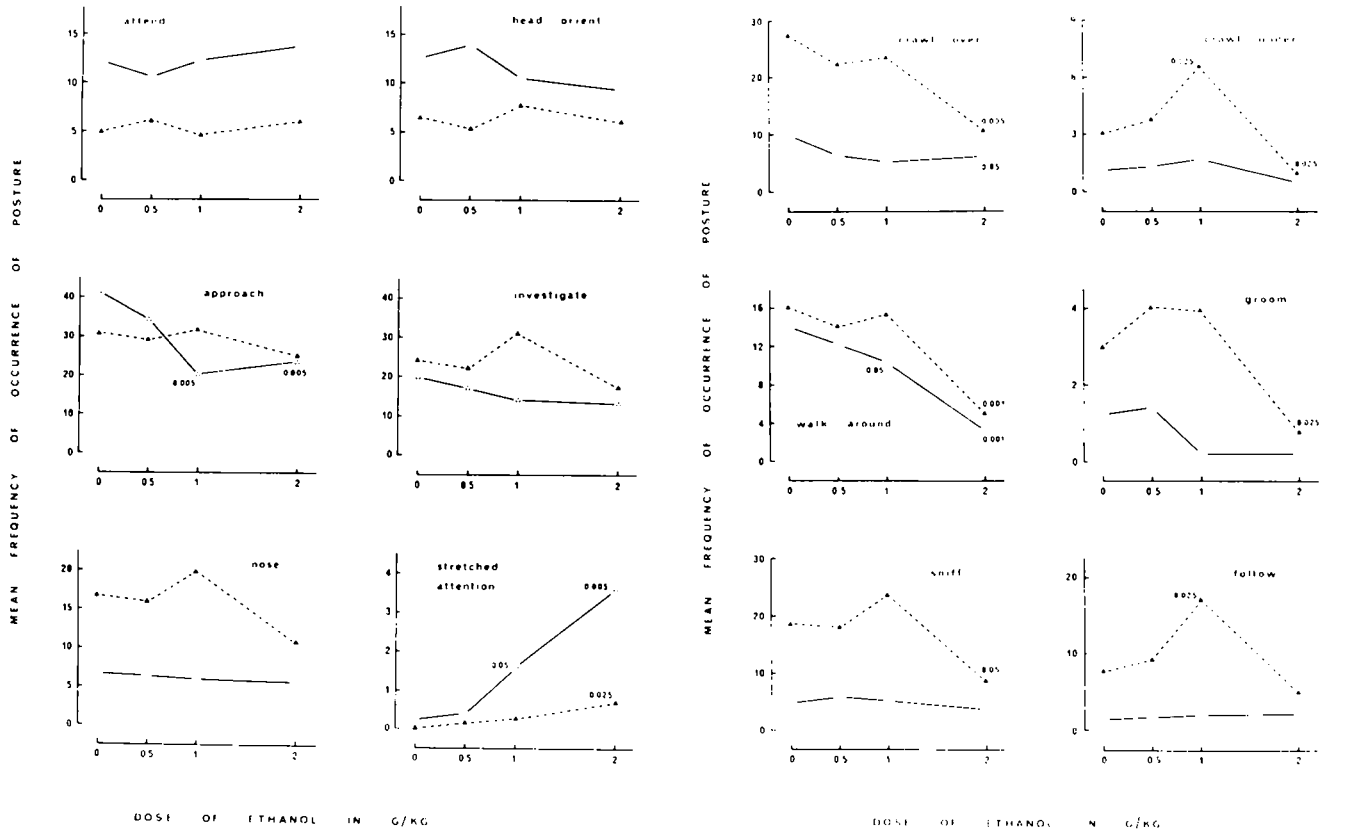

FIG. 3. Effect of ethanol on frequency of occurrence of various social/sexual acts and postures shown by singly-housed male mice during interactions with non-drugged "standard opponents." Open triangles, Swiss mice; closed triangles, TO mice.

injection are given in Table 2. There were no significant strain differences in the levels produced by the intermediate and high doses of ethanol; at the low dose however, the levels were significantly higher in the TO mice ($p<0.025$).

The expected increase in blood alcohol level with increasing dose administered was clearly evident in both strains ($p<0.001$).

DISCUSSION

The results do not provide any evidence for a potentiation of aggressive behaviour by ethanol; indeed, there appeared to be a dose-dependent suppression of most aspects of this behaviour in both strains. The baseline level of aggressive activities was quite high and therefore a potentiation may not easily be observed, although Kršiak [23] found increases in aggression in mice with both high and low aggressive baselines, and Miczek and Barry [26] found significant increases in dominant rats. Elements such as "attack" and "upright offensive" were in fact significantly decreased in Swiss mice even at 0.5 g/kg, a dose reported in other studies to enhance levels of aggression. In addition, "charge" and "aggressive groom" had low baselines, and no evidence of a potentiation was observed in these behaviours.

A major problem in psychopharmacological studies is assessment of the specificity of drug action on behavioural changes (particularly aggressive behaviour) i.e., are the changes due to the drug acting selectively upon the neural mechanisms mediating the particular behaviour, or to non-specific CNS depression. Kršiak and Borgesová [24] have shown that detailed ethological techniques help to elucidate the specificity of the observed drug effects, since postures similar in topography, but characteristic of different types of behaviour may not change in the same way at a given drug dose. Upright (or bipedal) postures are useful for assessing drug specificity, since these occur in all 4 categories of behaviour and involve a high degree of motor co-ordination in order to raise the upper part of the body. Examples include "rear" (non-social), "opponent rear" (social/sexual), "up-

TABLE 2

MEAN BLOOD ALCOHOL LEVELS (mg 100 ml), 20 MINUTES AFTER INTRAPERITONEAL INJECTIONS OF DIFFERENT DOSES (g/kg) OF ETHANOL IN TWO STRAINS OF MICE

Dose Injected	Swiss	"TO"
0.5	25	36*
1.0	97	105
2.0	256	263

*$p<0.025$, significantly different to Swiss mice.

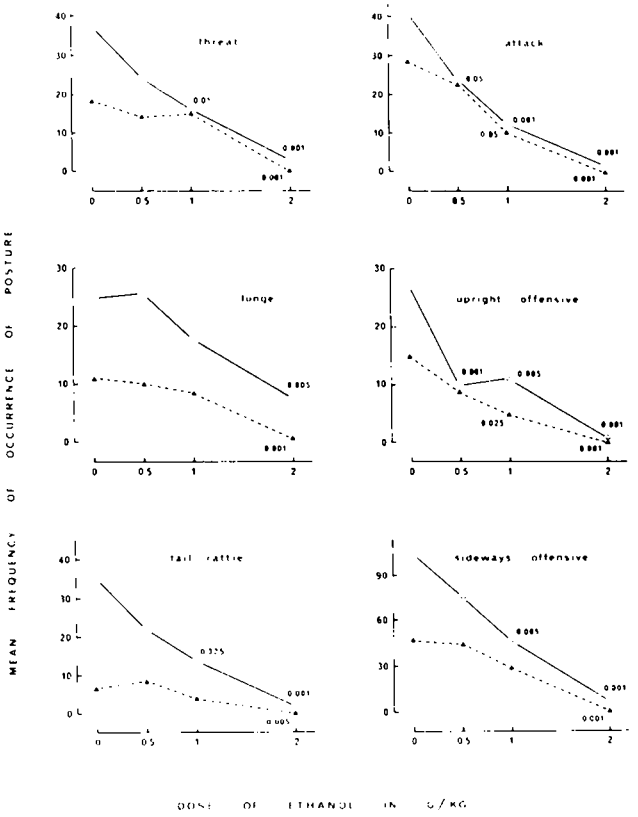

FIG. 4. Effect of ethanol on frequency of occurrence of aggressive acts and postures shown by singly-housed male mice during interactions with non-drugged "standard opponents." Open triangles, Swiss mice; closed triangles, TO mice.

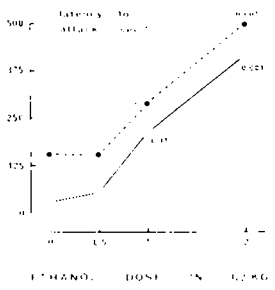

FIG. 5. Effect of ethanol on latency to attack shown by singly-housed male mice during interactions with non-drugged "standard opponents." Open circles, Swiss mice; closed circles, TO mice.

right offensive" (aggressive) and "upright defensive" (timid/defensive). Since "upright defensive" is potentiated at high doses of alcohol, the suppression of "rear" and "upright offensive" is unlikely to be due to a non-specific CNS depression.

A problem still remains, however, that even apparently selective drug-induced changes in behaviour may occur simply as a consequence of "competition" for available time in the 500-second trial, particularly when there are very large changes in certain behavioural activities as a result of drug action. These "see-saw" effects may work in two ways: the drug may directly potentiate some aspects of the behavioural repertoire leading to indirect decreases in other behaviours as a result of less time being available to perform these activities. Conversely, the drug may directly suppress certain activities, allowing more time for other behaviours, which may then be seen to be "potentiated."

The apparent lack of effect of alcohol on several acts and postures may be due to their low baseline levels in saline controls. Elements such as "chase," "aggressive groom," "circle," "bounce," "head groom" and "opponent rear" were all characterised by low baselines, and were unchanged by alcohol. This is not to say that alcohol has no effect on these elements: in models which encourage increased baseline frequencies, the drug may then be seen to modify them.

Alcohol did not seem to produce qualitatively different behavioural changes in the 2 strains studied; some elements were changed exclusively in a single strain, but the majority were either unchanged or changed in the same direction in both strains. The sensitivity of the Swiss strain seemed considerably greater than the TO mice however: significant behavioural changes were produced in Swiss mice at lower doses than in TO mice in the majority of non-social, aggressive and timid/defensive behaviours. This observed difference may not be due solely to differential sensitivites to alcohol in the 2 strains, but to differential effects of individual housing. If TO mice are less sensitive than Swiss mice to the effects of isolation, then the drug may have differential effects on behaviour in this situation. The results obtained for the screening trials did in fact show inter-strain differences in behaviour, but these same measures were generally similar in saline-injected controls in the drug trials. The only significant differences were higher levels of social/sexual ($p<0.05$) and lower levels of timid/defensive behaviours ($p<0.05$) in TO mice.

The differences in strain sensitivity to alcohol did not appear to be related to blood alcohol levels at the time of testing. No inter-strain differences were evident with the intermediate and high doses, which were the 2 generally effective doses.

The simple analysis of mean duration of time spent in 4 broad categories of behaviour showed that non-social and social/sexual behaviours were not significantly influenced by alcohol, except for an increase at the highest dose in non-social behaviour in TO mice; aggressive behaviour was suppressed in a dose-dependent fashion, while timid/defensive behaviour was increased in parallel. If conclusions were based entirely on this analysis, it could be deduced that ethanol had a simple effect on behaviour, making animals less aggressive and more fearful, but with non-social and social/sexual behaviours unaffected. The ethological analysis of acts and postures shows however, that many drug effects are not detected by the simple approach. For example, although Swiss mice showed no significant changes in time spent in non-social or social/sexual behaviour at any dose of ethanol, the postural analysis revealed that many elements within these categories were changed markedly.

The simplified analysis thus may fail to show the complete action of a drug on a particular category of behaviour; furthermore, it may even suggest an opposite effect of the drug to that revealed by the postural analysis. The simple analysis of time spent in non-social behavior suggested that

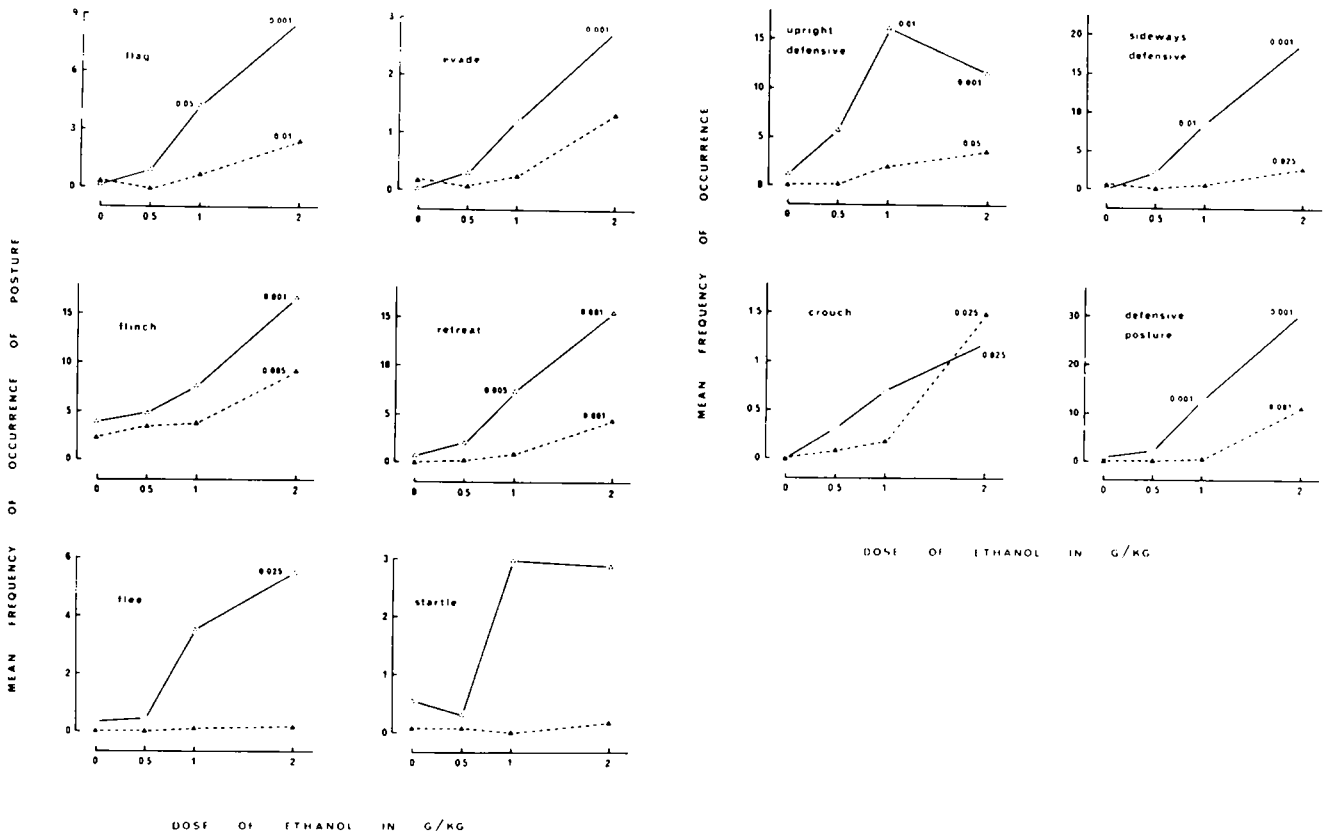

FIG. 6. Effect of ethanol on frequency of occurrence of timid/defensive acts and postures shown by singly-housed male mice during interactions with non-drugged "standard opponents." Open triangles, Swiss mice; closed triangles, TO mice.

TO mice were the more sensitive strain, since they showed a significant increase in duration, while Swiss mice showed no such changes. The postural analysis however, revealed that Swiss mice were in fact markedly more sensitive than TO mice, in terms of both the number of non-social elements of behaviour affected by alcohol, and the doses at which significant effects were observed. The significant increase in duration of this class of behaviour in TO mice appeared to be mainly due to the highly significant increases in "squatting" and "scanning."

The simplified analysis has the advantage of being fast and relatively easy to carry out, and may detect overall changes in broad categories of behaviour. In general, however, it fails to detect the many profound changes which occur within these categories. In view of this, detailed ethological analyses of acts and postures would appear to be essential in studies of this type in order to reveal the precise effects of drugs on behaviour.

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