apparently lose Sr while fossil aragonitic shells seem to gain Sr. If the biochemical evolution mechanism can be extended to calcitic shells, then the trend in this instance is toward less efficient extraction of Ca relative to Sr from seawater, because fossil calcite shells exhibit low Sr/Ca ratios. It is difficult to explain why aragonitic secreting molluscs have been evolving in the direction of greater shell purity while calcitic forms have not. Third, the evidently different behaviour of Sr in calcite and aragonite shells can be predicted from crystal chemistry. The large Sr ion may play a stabilizing part in the nine-fold coordinated Ca position in the aragonite lattice; hence the post-depositional increase. On the other hand, the Ca position in the calcite crystal lattice is a smaller site with six-fold coordination. The stability of calcite may therefore be enhanced by post-depositional loss of Sr. Pilkey and Goodell[5] have further demonstrated that the large Ba ion follows a similar path to Sr, and is enriched in fossil aragonitic shells and depleted in fossil calcitic shells.

Two indirect lines of evidence support the stabilizing role of Sr in the aragonite lattice. First, the only naturally occurring $SrCO_3$ compound, strontianite, has a crystal structure similar to that of aragonite rather than calcite. In addition, the negative free energy of formation of strontianite is slightly greater than that of aragonite ($-272{\cdot}00 \pm 0{\cdot}20$ kcalories/mole for strontianite compared with $-269{\cdot}57 \pm 0{\cdot}20$ kcalories/mole for aragonite)[8]. Second, data for distribution coefficients[9-11]

$$\left(D = \frac{\text{Sr/Ca aragonite or calcite}}{\text{Sr/Ca aqueous solution}}\right)$$

demonstrate that the average Sr/Ca ratio of fossil aragonitic shells is lower than the equilibrium ratio, whereas the average Sr/Ca ratio of fossil calcitic shells is higher than the equilibrium ratio. Ratios from fossils of both mineralogical types are closer to their respective equilibrium ratios than are those of Recent shells. In post-depositional changes before recrystallization the Sr/Ca ratio thus tends with age to approach the equilibrium ratio for both aragonitic and calcitic specimens. These relationships hold whether calculations use the Sr/Ca ratio of normal marine waters ($9{\cdot}5 \times 10^{-3}$) or known values of Atlantic Coastal Plain pure waters ($6\text{–}9 \times 10^{-3}$) (ref. 12).

Although the distribution coefficients are only known accurately[9,10] for 90°–100° C, rather than the 20°–30° C that probably prevailed during the alteration process, the distribution coefficients are nevertheless higher at lower temperatures[12]. Any higher distribution coefficient in the case of aragonitic shells will not invalidate our conclusion, but could affect the case of calcitic shells. For example, when the Sr/Ca ratio of marine waters is combined with a distribution coefficient of 0·13 (upper limit from Oxburgh *et al.*[11] for 30° C), the equilibrium ratio of $1{\cdot}2 \times 10^{-3}$ is between the fossil and Recent averages (Table 1). But ratios from Coastal Plain waters are probably[12] nearer 8×10^{-3}, so the conclusion that calcites approached the equilibrium ratio during post-depositional alterations is probably still valid.

We believe the evidence strongly indicates that the Sr/Ca ratio of fossil mollusc shells may be significantly altered by inorganic processes before recrystallization. A biochemical evolutionary trend in Sr uptake could possibly be superimposed on the observed post-depositional alterations. It seems difficult, however, to differentiate biochemical factors from inorganic diagenetic effects.

One consequence affects geochemical tools applied to carbonate materials. Radiometric dating of shell material, as well as oxygen and carbon isotope and trace element studies, are based on the assumption of unaltered composition. The post-depositional fractionation of isotopes in unrecrystallized calcareous invertebrate skeletal material therefore needs urgent investigation.

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Genotype, LSD and T-maze Learning in Mice

Variation in T-maze learning in mice is determined by genetic and environmental (treatment) effects and interactions among them[1-4]. Lysergic acid diethylamide-25 (LSD-25) affects attack and inhibition behaviour, gross locomotor activity and swimming time in a water T-maze[5-7]. Strain differences in aggressive behaviour reaction to LSD, that is to say, a genotype × treatment interaction, have been suggested[5]. Here we evaluate the effect of LSD-25 and genotype on T-maze learning and demonstrate a significant genotype × treatment interaction for some components.

A complete diallel cross, including inbreds and reciprocals, was made among four inbred lines: A/HeJ, C3H/J, C57BL/J6 and SWR/J. Six single pair matings were made for each line and cross. Each pair was housed in a plastic cage (8 × 11 × 5 inches) with commercial bedding and food (Purina Lab Chow pellets) and water supplied as required. The cages were assigned by random numbers to a position in a standard mouse room. Litters were weaned at 21 days and caged as a group until tested at 35 days. There were five to eleven mice in each genotype × sex × treatment subclass; 464 in all. Half the mice of each sex in each litter were given 0·4 mg/kg body weight LSD tartrate (Sandoz batch 65002) intraperitoneally 2 min before the start of the test, and the other half were given an equivalent volume of a placebo (Sandoz batch 65045). The LSD solution and placebo were diluted with normal saline so that a volume of 0·1 ml. to 0·5 ml. was injected.

We used a single unit electroshock alley T-maze with sides of opaque acrylic plastic and hinged tops of clear acrylic plastic. The floor consisted of 1/8 inch diameter stainless steel rods 3/8 inch apart. The start box was 2 × 4 × 4 inches, the runway was 2 × 8 × 4 inches and each stem of the cross arm was 2 × 8 × 4 inches. A guillotine door separated the start box and runway. Direct current was passed through the floor of the start box, runway and to either stem of the cross arm by an alligator clip. The current could be varied from 0·15 mA at 35 V to 0·50 mA at 50 V.

Each mouse was removed from its cage, identified, weighed, injected with LSD or placebo and rested in a

separate cage for 2 min before testing. The test involved placing the mouse in the start box for 5 s before raising the guillotine door. Five seconds after the door was raised, 0·15 mA at 35 V was applied. Corrections were permitted and the animal was required to reach the correct stem (no current) before a trial was considered complete. A correct response consisted of the animal moving from the start box to the correct stem without error. The test ended when the criterion of nine consecutive correct trials was satisfied. If a mouse failed to enter the correct stem within 55 s after shock was initiated, the level was raised to 0·5 mA at 50 V and the latency for the trial recorded as 60 s. Forty mice made an error on or after the twenty-first trial. They were judged untrainable and the total number of trials recorded as thirty. There were twenty-one males and nineteen females in this group. Twelve of the forty received placebo and twenty-eight LSD. The procedure adopted would thus tend to minimize the effect of LSD with respect to the statistical analyses.

The response measures analysed include (1) the number of trials to criterion, (2) the median latency for all trials, (3) the median latency for the final nine trials, (4) the percentage of trials requiring stimulus, and (5) the percentage of errors. The mathematical model describing the data is an extension of that formulated by Henderson[8] and includes the effects of treatment, sex, inbred lines, heterosis, general combining ability, specific combining ability, maternal ability, residual reciprocal effects and the appropriate interactions. The linear contrasts among the linecross means defining the main effects are described by Griffing[10]. A least squares analysis of variance[9] was completed.

Our conclusions are: (1) The effect of LSD-25, differences among inbred lines, and differences in general combining ability among lines are highly significant for all responses. (2) Heterosis is highly significant for all responses except the number of trials to criterion. (3) The significant interactions include: (*a*) treatment × heterosis for the number of trials to criterion, percentage of trials stimulated and percentage of errors; (*b*) treatment × inbred lines for the number of trials to criterion and median latency for all trials; (*c*) treatment × general combining ability for the median latency for all trials. (4) All remaining main effects (sex, maternal ability, specific combining ability, residual reciprocal effects) and interactions involving them are small and not significant. They were removed from the model and the analysis repeated to obtain more efficient estimates of the significant effects.

Least squares means for the various comparisons, except the treatment × general combining ability and treatment × inbred line interactions, are given in Table 1.

LSD-25 greatly inhibited T-maze learning in all responses. The median latency for the final nine trials was increased by 57·6 per cent. The percentage of trials requiring stimulation was least affected but was increased by 10·8 per cent.

Table 1. LEAST SQUARES MEANS FOR SIGNIFICANT EFFECTS (ADJUSTED FOR UNEQUAL NUMBERS BY LEAST SQUARES)

Classification	Number trials to criterion	Median latency for all trials	Median latency for final nine trials	Per cent trials stimulated	Per cent errors
Treatment:					
Placebo	15·3	8·3	6·6	84·5	16·8
LSD-25	19·2	11·5	10·4	93·6	22·4
Heterosis:					
Inbreds	—	11·3	10·1	93·2	18·4
Crossbreds	—	8·4	6·8	85·2	20·7
Inbred lines:					
A/HeJ	18·2	16·7	16·0	96·7	19·6
C3H/J	15·1	14·3	11·7	95·5	13·8
C57/BL/J6	13·0	8·1	8·0	96·7	13·8
SWR/J	23·3	6·2	5·0	78·8	27·7
Genic breeding value for crossing:					
A/HeJ	14·2	10·9	9·7	92·5	16·7
C3H/J	16·1	10·6	7·7	82·8	15·4
C57BL/J6	15·1	8·4	7·9	93·8	17·6
SWR/J	19·9	3·8	−1·0	65·7	35·5
Treatment × heterosis:					
Placebo × inbred	15·1	—	—	90·4	14·8
Placebo × crossbred	15·6	—	—	77·4	19·0
LSD-25 × inbred	20·0	—	—	95·5	22·4
LSD-25 × crossbred	18·4	—	—	91·5	22·4

The least squares means of all hybrids were compared with the means of all inbreds and interpreted as a measure of heterosis. The absence of heterosis for number of trials to criterion and its existence for both latency measures are consistent with our previous results[11]. Crossbreds moved more rapidly and required fewer stimuli, but made more errors than inbreds. This may have been caused by greater exploratory behaviour of crossbreds[12].

LSD-25 increased the number of trials required to reach criterion for crossbreds by 2·8, from 15·6 to 18·4, while for the inbreds the increase was 4·9, from 15·1 to 20·0. LSD-25 thus had a greater adverse effect on inbreds than on crossbreds. The percentage of errors committed by inbreds was increased from 14·8 with placebo to 22·4 with LSD-25, while the increase for crossbreds was from 19·0 to 22·4 per cent. LSD-25 also had a greater effect on crossbreds for the percentage of trials stimulated. For all responses the interaction was the result of a larger detrimental effect of LSD-25 on the genotype (inbred or crossbred), demonstrating higher learning ability with the placebo.

The highly significant differences among inbred lines were expected[11]. The treatment × inbred line interaction for the number of trials to criterion was largely a result of the extreme adverse effect of LSD on the A/HeJ line, where LSD-25 increased the number of trials from 12·9 to 23·4. All other lines were increased, but by a much smaller number.

The interaction for median latency for all trials was caused by a large effect of LSD-25 on the C3H/J line in which LSD-25 increased the median latency from 9·7 to 19·0 s. There was no difference between treatments for the SWR/J line and only small differences for the other two.

General combining ability effects are assumed to be one-half the additive genetic value (breeding value) of the line[9]. The SWR/J line was the poorest inbred line with respect to the number of trials to criterion and percentage of errors, and was also the poorest line for crossing; but it was the best performing inbred line with respect to median latency and percentage of trials requiring stimulation, and performed best in crosses. The breeding value of the SWR/J line was increased only slightly when LSD-25 was administered, but it increased markedly for the other three lines.

These data suggest that the major genetic source of variation in electroshock alley T-maze learning in mice results from additive genetic variance. LSD-25 generally inhibits learning ability. The few significant interactions were always caused by an exceptionally greater negative response of a line or cross to LSD-25. In no instance was learning ability enhanced by LSD-25.

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