control group in the table). With smaller doses of GTG the dose-response relationship was not linear, as shown in the figure, B. We were able partially to reproduce the protective effect of reserpine by methiothepin (1 mg/kg) and 2-chlorocinanserin ($SQ_{10,631}$), drugs which are serotonin-receptor blockers[12] and with a combination of nialamide (500 mg/kg) + DL-α-methyldopa (500 mg/kg) that, according to Corrodi[13], blocks the accumulation of serotonin (5HT) and norepinephrine but does not affect dopamine (DA) content in mouse brain. The protective effect of methiothepin was increased when it was given in combination with pimozide (0.5 mg/kg). In the replication of the reserpine effect, the best results were obtained with $SQ_{10,631}$, as given in the table. The reserpine effect was not reproduced with monoamine synthesis blockers and catecholamines receptor antagonists. We were not able to render reserpinized mice vulnerable to GTG either by serotoninergic and dopaminergic agonist, alone or in combination, nor by insulin.

One of the interpretations of this finding would be that we might be dealing here with a permissive factor which, in addition to insulin, is necessary for GTG to accumulate in and destroy the VMH. This factor could possibly be 5-HT and DA intervening with insulin in a chain of biochemical processes permitting the capture of GTG and of glucose by VMH. To a certain extent, the stimulation of appetite by 5-HT receptor blocking agents[14] and the anorexia produced by serotonin-like drugs[15,16] supports this view.

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Spontaneous maze ambulation in two mouse strains

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Summary. A simple device is described, which permits us to quantify several parameters of spontaneous behaviour of small animals. Using this device with mice we obtained statistically satisfactory results, showing a strong genetic influence on the behavioural characteristics tested.

An increasing number of psychobiological investigations on learning performances, memory processes and behavioural developments in mice require an adequate training apparatus. Various devices; behaviour equipments, 'torture chambers' such as the shuttle box[2-4], the running wheel[5], the Deutsch carousel[6], the photoswitch activity cage[7,8] etc. have been used, in which the animal is subjected to different escape and avoidance mechanisms, electric shocks, motion restriction, and deprivation of food and water[3,9,10].

The use of an aversive stimulus might be responsible for emotional components in subtle experiments on memory and learning in mice which can be variously interpreted. This paper describes a training apparatus which allows free exercise without any external stimulation, food and water deprivation or light or electric-shock conditioning.

Apparatus. As depicted in figure 1, the training apparatus (the apparatus is available from Medical Research Co., F-91160 Longjumeau) used for the study is composed of a 'departure' and an 'arrival' cage, both supplied with food and water, separated by a squared maze (40 × 40 cm) with multiple corridors. The latter can be modified as desired by rearrangement of walls and gates. There is a direct connection between the arrival cage and the departure cage by means of a 1-way tunnel. 1-way gates in the maze prevent the mouse from coming back.

From the departure cage, the mouse to be tested can enter the maze via a 1-way gate which will prevent it from returning to the departure cage. Entrance into the maze is detected by an opto-electronic unit which activates an electronic clock. When the mouse has found the exit and leaves the maze by a 1-way gate, it is detected by another opto-electronic unit which inactivates the electronic clock. At this moment, a printer prints the number of sec during which the mouse remained inside the maze, and the time of day in h and min. The mouse is then in the arrival cage and can return freely to the departure cage, by means of an external 1-way tunnel. A new round trip can be performed as often as the mouse decides.

Results and discussion. 2 identical mazes were used simultaneously, under the same external conditions (air-condi-

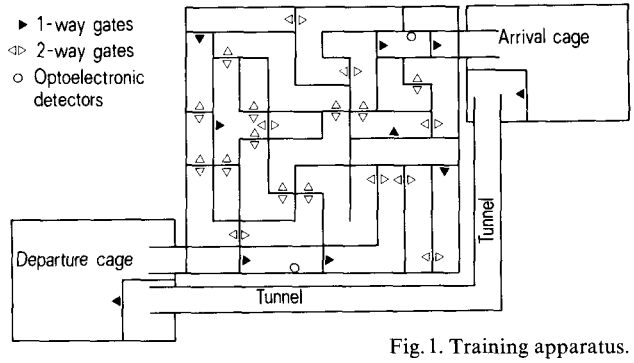

Fig. 1. Training apparatus.

Mean numbers of roundtrips per mouse over a 24-h test

	A/Sn female, 2–3 months of age, 2 experiments pooled	B10.Br, female, 2–4 months of age, 3 experiments pooled	Statistical difference*
Total number of tested mice	19	27	
Total roundtrips**	57.3± 11.5	93.2± 38.1	$p<0.001$
Roundtrips performed in less than 50 sec**	15.5± 7.8	51.0± 26	$p<0.001$
Roundtrips performed in less than 20 sec**	4.2± 3.3	24.3± 18.5	$p<0.001$
Roundtrips performed in less than 50 sec during the first 6 h of the test**	1.3± 1.6	18.8± 11.9	$p<0.001$

* Student's t-test; ** ± SD.

tioned, light scheduled and noiseprotected room). In each maze, 1 mouse was trained during 24 h (the run being always started at noon). Several mouse strains were used and compared with one another. Mice of a given strain were alternately placed in one maze or the other, to prevent any 'maze effect'. From the printer, the following data were collected for each individual mouse: total number of round trips in 24 h, number of round trips performed in less than 50 sec or 20 sec over the same 1-day period, and number of 'rapid' round trips (less than 50 sec) performed during the beginning of the test, namely during the first 6 h after the starting time.

A typical comparison is depicted in the table which is computed from the results of several separate experiments which were made under the same conditions with age- and sex-matched mice. More than 90% of the mice of any strain did enter the maze, and found the exit. All of these returned to the departure box and made new round trips. However, the total number of runs did differ considerably according to strain. Not only did the total number of round trips show a genetic influence, but also the length of time necessary to cross the maze. Assuming that mice of any strain occasionally rested for a very long time inside the maze (i.e. > 5,000 sec), the number of round trips performed within shorter period of time (< 50 sec, < 20 sec) were also computed. The table shows that this criterium gives still sharper discrimination of the genetic influence than the 'total round trips' counts did (the shortest crossing time recorded was 5.8 sec by a B10.Br mouse).

A still more discriminating criterium is the record of short-time round trips counted during the earliest period of the test, for instance during the first 6 h (which is supposed to be the learning period). The difference between the 2 strains shows still more dramatic differences, varying from an average of less than 2 round trips per mouse in the case of A/Sn to more than 18 round trips in the case of the B10.Br (table).

If we consider the behaviour of the mice of both strains as a function of clock time, from the beginning to the end of the session, one observes a decrease in activity in both cases. Representative time charts are shown on figure 2. This decrease of activity could be attributed to habituation: other experiments (unpublished) show that if the same mouse is left several consecutive days in the maze, the numer of daily round trips stabilizes to a value less than that of the 1st day.

Figure 2 also depicts a 2–3-h period of almost complete inactivity, which is observed in the morning of all 24-h experiments with both strains. Also, it shows the difference between B10.Br and A/Sn mice as to their performance during the first 6 h of the test.

To conclude, we present here a device which permits us, within the statistical dispersions inherent to the nature of the parameters studied, to quantify some aspects of the behaviour of mice. The originality of this new system is to eliminate the influence of purely emotional events which usually accompany behaviour tests which use punishment and/or reward systems. In the present case, the quantified events are controlled by the subjects' decisions and no external action is necessary for their activation. In this respect, spontaneous learning[11] seems a better model for studying agents which can affect human behaviour.

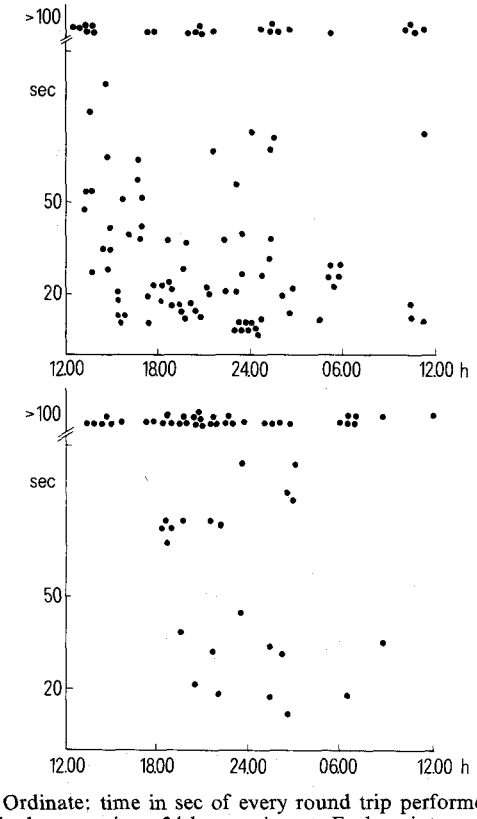

Fig. 2. Ordinate: time in sec of every round trip performed by an individual mouse in a 24-h experiment. Each point represents 1 round trip. Abscissa: clock time. Upper part: 1 representative B10.Br mouse. Lower part: 1 representative A/Sn mouse.

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1 We wish to thank Mr R. Laplace for technical help, Mr J.P. Arnould for electronic work as well as I.N.S.E.R.M. - SCR 3.

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