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# The quantitative measurement of motor inco-ordination in naive mice using an accelerating rotarod

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A simple modification of the standard rotarod apparatus is described which eliminates the necessity of time-consuming training and consequently gives a truer measure of motor co-ordination since any effects on memory are avoided. The sensitivity and reproducibility of the procedure are much greater than those obtained with constant speed rotarods and less animals are required to obtain statistically significant results.

THE performance of untreated naive mice on the usual constant-speed rotarod (Dunham & Miya, 1957) is very variable. Accordingly some form of preliminary training (to eliminate very low times) and the introduction of a time limit for any one trial (to eliminate very high times) are necessary to obtain satisfactory measures of performance after drug administration when both graded-response (Kinnard & Carr, 1957) and quantal (Janssen, Van de Westeringh & others, 1959) assay methods are used. In addition to being time-consuming, such procedures are undesirable since (a) drugs might affect memory rather than motor co-ordination in trained mice and (b) the artificial time limit reduces the sensitivity of the method. The prototype apparatus described is an accelerating rod that eliminates these problems. It was recently demonstrated to the Joint British and German Pharmacological Societies Meeting held at Cambridge (September, 1967).

## DESIGN OF THE APPARATUS

The rotating rod is a steel bar (18 inches long, $\frac{3}{4}$ inch diameter) covered by rubber tubing to give a final external diameter of $1\frac{1}{2}$ inches and divided into five 3 inch compartments by means of aluminium discs (10 inches diameter). Each end of the bar is run in a ball race. The rod is coupled *via* a 100:1 reduction gearbox to a permanent magnet DC motor (Pullin, 18 PM, 28 V) connected in series to a 100 ohm toroidally wound resistor (Birch and Co.). This resistor is itself driven by a kymograph motor so that a change in final speed from 2 rev/min (maximum resistance) to 50 rev/min (minimum resistance) is obtained over a period of $5\frac{1}{2}$ min. A diagram of the electrical circuit is shown in Fig. 1.

The speed-time relation in an ideal apparatus should be linear from zero to maximum speed but in the relatively cheap construction described it is not linear (Fig. 1 inset). A specially graded resistor would be required to produce a constant change in speed although the results obtained with the existing apparatus indicate that the bias introduced as a result of non-linear acceleration is not a serious problem.

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In operation mice are placed on the stationary rod with the resistor in the position of maximum resistance. When the drive to the resistor is activated, the rod slowly accelerates so that even the most agile mouse is unable to stay on the rod for more than a few minutes.

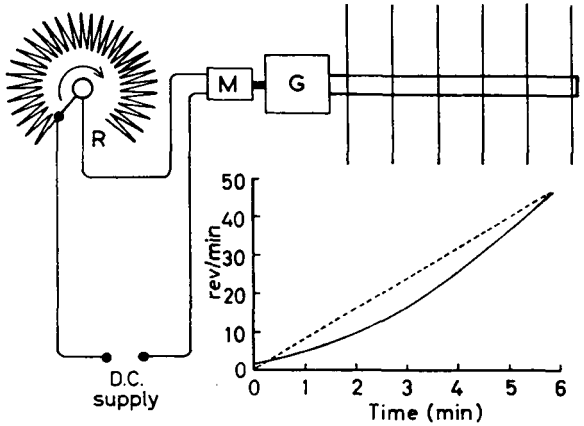


FIG. 1. Diagram of the basic arrangement for the accelerating rotarod with inset showing the actual acceleration (solid line) obtained compared with the ideal (broken line). R = variable resistance; M = motor; G = 100: 1 reduction gearbox.

TABLE 1. MEAN PERFORMANCE TIMES OF DIFFERENT GROUPS OF 25 UNTREATED NAIVE MICE TESTED ON THE ACCELERATING ROTAROD OVER A PERIOD OF 3 MONTHS. Figures are in sec ± standard errors of the means

| | | |
|---|---|---|
| 170·4 ± 9·3 | 148·2 ± 10·3 | 164·8 ± 9·5 |
| 154·8 ± 11·4 | 141·0 ± 11·0 | 151·3 ± 11·6 |
| 158·6 ± 9·4 | 177·0 ± 9·9 | 157·9 ± 11·1 |
| 164·6 ± 7·9 | 135·7 ± 10·4 | 171·3 ± 12·5 |

RESULTS AND DISCUSSION

Groups of 25 male albino Swiss mice (18–23 g) were used. Table 1 shows the mean performance times (sec) of 12 such groups of untreated naive mice taken randomly over a period of several months from different stock cages. Although significant differences can be demonstrated between the lowest and highest measurements, there were no differences between groups taken from the same stock cages. Under usual experimental conditions, therefore, where control and test animals are taken from the same stock population, naive mice can be used with complete confidence in the reproducibility of performance times. As a result, the new apparatus is capable of detecting statistically significant drug-induced changes in motor co-ordination at much lower dose levels and using fewer animals than those required with the constant speed rotarod (Kinnard & Carr, 1957; Kuhn & Van Maanen, 1961; Posner, Hearst & others, 1962). The dose-effect curves for some of the drugs so far tested are shown in Fig. 2 and may be compared with equivalent curves obtained from experiments on non-accelerating rods in the literature already quoted.

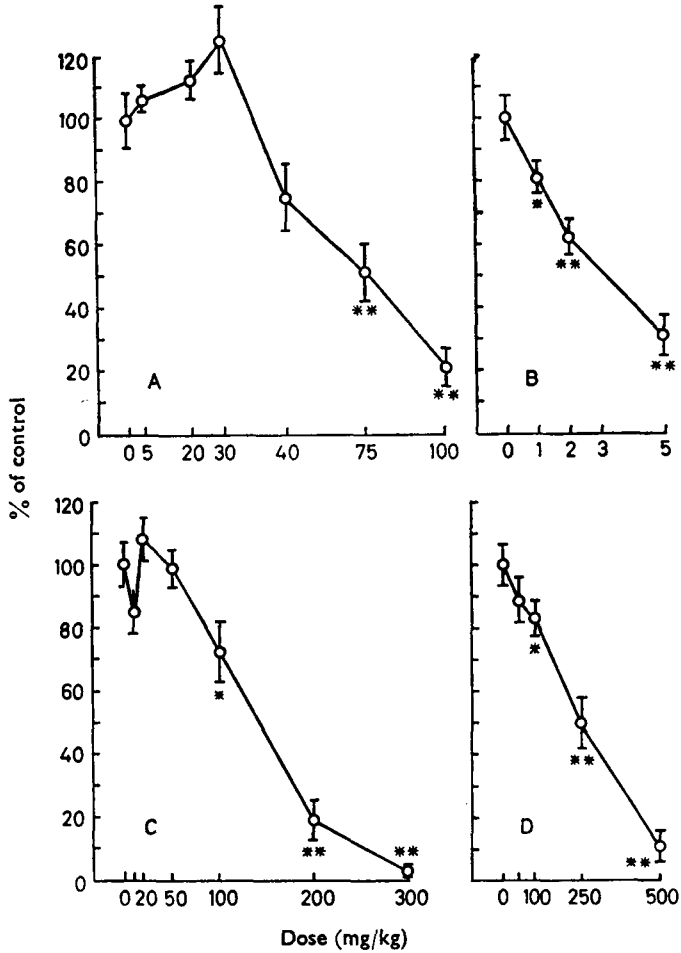


FIG. 2. The influence of phenobarbitone (A), chlorpromazine (B), meprobamate (C) and ectylurea (D) on the performance of naive mice on the accelerating rotarod. Each point represents the mean ± standard error (vertical line) of 25 observations expressed as a percentage of the performance of the control group. Doses in mg/kg administered intraperitoneally 30 min (A) and 20 min (B, C, D) before testing. A and B dissolved in saline, C and D suspended in 1·5% sodium carboxymethyl cellulose; control groups received appropriate solvent.
* $P < 0.05$. ** $P < 0.001$.

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