INVESTIGATIONS OF THE SENSORY BLOCKADE EFFECT OF PERINEURALLY INJECTED ETHANOL ON THE TAIL NERVE OF THE MOUSE

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SUMMARY

The effect of an alcohol block on the conduction of sensory stimuli in the tail nerve of the mouse was investigated using the perineural injection of solutions of ethanol (35, 40 and 45%). One hundred and fifty white mice of either sex were given 2 x 0.03 ml of the relevant alcohol solution into both sides of the tail. Before and after the injections repeated sensory conduction measurements were made using the rat tail method. Using 35% ethanol a temporary block of pain conduction could be achieved in both sexes. By increasing the concentration to 40 or 45%, a prolongation of the blocking effect and an increase in the accompanying increase of the pain threshold was observed in some animals. On the other hand, some animals, temporary motor paralysis occurred following 35% ethanol, and this effect became more frequent and severe using 40 and 45% ethanol. A further increase in the alcohol concentration was not possible because of the occurrence of anatomical changes in the tails of the experimental animals.

Since Schlösser’s first reports (1903, 1906, 1907) of the treatment of neuralgia by the perineural injection of alcohol, there have been many published accounts of the results obtained in the treatment of painful conditions. Normally, alcohol concentrations of at least 70% have been used to produce conduction block. However, there has been no general agreement as to which concentration should be used to block conduction in mixed peripheral nerves. Indeed, many authors have rejected completely the use of ethanol because of the possibility of motor paralysis following too high concentrations on the one hand, and persistent neuritis without reliable pain relief following too low concentrations on the other.

The purpose of the present investigation was to determine the minimal concentration of ethanol required to cause sensory block and the duration of its effect; and the effect of increasing the concentration of ethanol on the duration of the sensory block.

METHODS

The sensory blocking effect of 35, 40 and 45% ethanol in aqueous solution was investigated on the tail nerve of the mouse using the “Rat tail method” described by Herr, Nyiri and Pataky (1953), Ther (1953) and Herr (1958). A focused beam of light was applied to the proximal third of the tail to produce an adequate pain stimulus (fig. 1). The reaction times of the experimental animals were noted.

Fig. 1. Device for measuring analgesia (Ther, 1953) (manufacturer: J. F. Bundschuh, Darmstadt).

Three hundred and ten white mice of either sex were studied. A preliminary study comprised 160 white mice of either sex, weighing 25–35 g, using 10, 20, 30, 40 and 50% ethanol solutions, and 1% xylocaine solution. The remaining 150 white mice
were studied in the main investigation described here. Their average initial weight was similar to that of the first group.

The groups were treated as follows:

Group 1: Control group, untreated.
Group 2: Comparison group; injection of sodium chloride solution (NaCl) 0.9%.
Group 3: Test group; injection of 35% ethanol.
Group 4: Test group; injection of 40% ethanol.
Group 5: Test group; injection of 45% ethanol.

The average normal reaction time of all the animals was determined by two preliminary measurements. The animals in groups 2–5 then received two perineural injections of 0.03 ml of the relevant test solution into the paired tail nerves at the level of the base of the tail. The subsequent measurements of sensory blockade were made in Groups 1–5 after 24 h, and then weekly until the 7th week. Total sensory blockade may be assumed when the pain threshold is not reached within twice the baseline reaction time (Herr, 1953). Because of the scatter of the individual reaction times a value of 12 s was accepted, a time identical to the maximum stimulus duration.

RESULTS

The control reaction times of the 160 experimental animals in the preliminary investigation are shown in figure 2. The frequency distribution of the individual reaction time conforms to a Gaussian distribution, with a peak at approximately 4.8 s. The mean control reaction time of these animals was 4.79 (SD 0.47) s. It was observed that the females, with an average of 4.67 s compared with 4.91 s for the males, had a lower pain threshold. This difference was statistically significant ($P \leq 0.01$).

The mean reaction times of the control group varied between 4.56 s (initial value) and 5.22 s (after 6 weeks). It is apparent from the shape of the time–response curve that the pain threshold reaches a maximum in the 6th week (fig. 3). At the end of the investigation, after 7 weeks, the mean reaction time for the group was 5.07 s, 0.51 s more than the baseline value.

The injection of a solution of sodium chloride had no significant effect on the pain threshold (fig. 4).

In the group which received 35% ethanol there was, in all the animals, at 24 h after the injection, a complete block of pain conduction. One week later three of the 30 animals continued to have a total sensory blockade; at this time two of the animals showed signs of motor paralysis in the tail. After this the pain threshold in all animals decreased gradually, so that after 7 weeks the mean reaction time in this group was 5.03 s, 0.21 s above the initial value of 4.82 s (fig. 5).

The results obtained in those animals treated with 40% ethanol were similar to those of group 3 (fig. 6). However, both the sensory and the motor blockade
were more obvious and persisted longer. For example, 1 week after the injection, 11 of the 30 animals showed a complete blockade of pain conduction, and nine of the animals showed motor paralysis of the tail. Seven weeks after the injection the mean reaction time for the group was 5.21 s, 0.18 s greater than the initial value of 5.03 s.

The baseline reaction times in the group treated with 45% ethanol were higher than those of the other groups (fig. 7). After 24 h all the animals showed both a complete sensory blockade and also complete paralysis of the tail muscles. One week after the injection, 13 of the 30 animals continued to have a total sensory blockade, and, in 18, motor paralysis could be demonstrated. After 2 weeks four of the animals showed motor weakness of varying degree, but only one showed a complete sensory conduction block. Seven weeks after the injection the mean reaction time of the group was 5.32 s, 0.5 s greater than the initial value. Furthermore, in some animals in this group anatomical changes occurred, such as a doughy swelling of the tail, and small ulcers which, however, healed with scarring after a maximum of 4 weeks.

DISCUSSION
The sensory blockade resulting from the perineural injection of various ethanol solutions into the tail nerve of the mouse was reversible in all cases. The rate of recovery varied between animals and, with one exception, after the 2nd week there was only a small increase of the pain threshold. The differences between the individual groups in the amount of sensory block present after 1 or 2 weeks, and the subsequent differences in the rate of recovery from the increases in pain threshold demonstrated the varied effects of the different concentrations. The recovery curves of Groups 4 and 5 were only slightly different, but showed a considerably greater effect on pain than that seen in Group 3.

The fact that a slight increase in reaction time after the 4th week was observed in both the control and the comparison groups demonstrated that the slightly increased reaction times found in Groups 3, 4 and 5 after the 4th week were of no significance.

It seems noteworthy that relatively low concentrations of ethanol (35%) caused temporary motor
weakness. After the injection of 45% ethanol this motor paralysis persisted for up to 14 days. The anatomical changes in the tail of the experimental animal after the alcohol injections were striking. They were already so marked with the use of 45% ethanol that investigations using higher concentrations could not be considered.

Therefore, it was not possible, using the "Rat tail method" in mice, to determine a concentration which would be capable of producing longer-lasting or irreversible sensory blockade. The results of the present study suggest that it is possible to produce sensory block in small mixed peripheral nerves using solutions containing 40–45% ethanol and that those will not cause severe, irreversible motor lesions.

REFERENCES