release of acetylcholine by adrenaline could occur under physiological conditions.

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Modification of the Auditory Flutter Fusion Threshold by Centrally Acting Drugs in Man

PERCEPTUAL fusion of intermittent random noise stimuli at critical frequencies in man was first reported by Miller[1] and Miller and Taylor[2], and confirmed by Symmes, Chapman and Halstead[3]. The process is analogous to visual flicker fusion. The critical interruption rate at which fusion occurs is termed the "auditory flutter fusion threshold".

In view of the sensitivity of visual flicker fusion thresholds to the actions of psychotropic drugs, it is perhaps surprising that the psychopharmacology of auditory flutter fusion threshold has received little attention. Only Eysenck and Easterbrook[4] appear to have explored this field and they were unable to demonstrate any effects of sodium amylobarbitone (90 mg), dexamphetamine (5 mg) or meprobamate (100 mg) on auditory flutter fusion threshold. However, the interruption rates of their auditory signal varied in the relatively large steps of ten interruptions per second (i.p.s.) so that small changes in the threshold might have escaped detection.

We have found that the auditory flutter fusion threshold was highly sensitive to centrally-acting drugs, and this communication reports the actions of amylobarbitone, chlorpromazine and perphenazine.

The technique was a modification of that used by Miller and Taylor[2]. A random noise signal, which could be interrupted at rates of between 1·5 and 275 i.p.s. (on–off ratio 9 : 1), was used at an intensity of 55 db (re. 0·0002 dynes/cm^2). The interruptions were automatically switched on and off at intervals of 1 sec so that the signal, presented binaurally to the subject, consisted of alternating 1-sec periods of interrupted or continuous noise. For each test the starting interruption rate was 100 i.p.s. and then the signal was presented in a sequence of decreasing interruption rates. The critical descending auditory flutter fusion threshold was taken as the fastest interruption rate at which auditory flutter (that is, the interruptions) could be distinguished and below which consistent positive flutter responses were reported by the experimental subject.

Six normal healthy male subjects (aged 21–30 yr.) participated in each of the double blind cross-over trials. Subjects were allowed a light breakfast. The active compound (amylobarbitone—100 mg, or chlorpromazine—25 and 50 mg, or perphenazine—2 and 4 mg), or its placebo control, was administered by mouth between 9 and 10 a.m. at 7-day intervals. On each treatment day, three threshold determinations were made, at 5-min intervals, before treatment was administered and at 90 and 180 min later. Changes in the mean thresholds from the control values on the active and placebo treatments were compared using the method of analysis of variance for factorial designs and Student's two-tailed 't' test (Snedecor[5]).

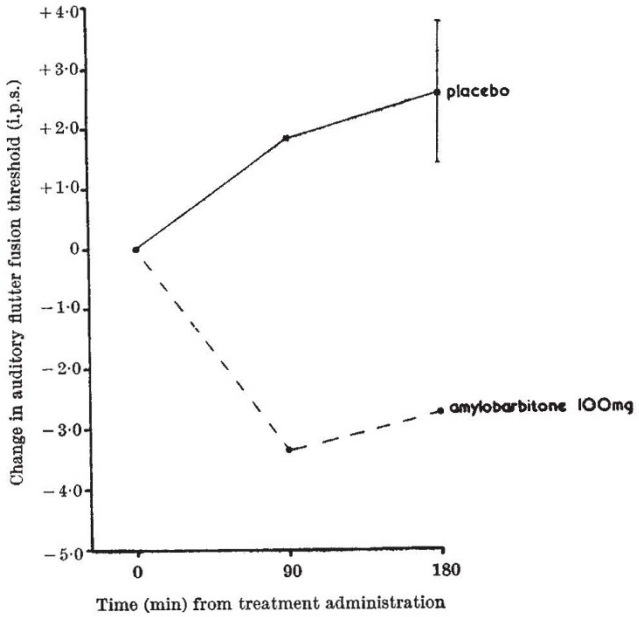

Fig. 1. The effect of amylobarbitone (100 mg) and placebo treatment on the descending auditory flutter fusion threshold. The changes in the mean thresholds are from those recorded before treatment (six subjects). ▮, Standard error of the mean

The changes following amylobarbitone (100 mg) are illustrated in Fig. 1. The pretreatment mean thresholds were 42·93 i.p.s. for the placebo and 43·10 i.p.s. for the amylobarbitone treatment. The usual rise in the auditory flutter fusion threshold over the 180-min period on the placebo is seen (continuous line). After amylobarbitone (broken line), the threshold was lower than after the placebo both at 90 min (by 5·17 i.p.s.) and at 180 min (by 5·27 i.p.s.), and analysis showed that this depression was significant:

For the overall difference between placebo and amylobarbitone treatment effects, $F_{1,15} = 20{\cdot}03$, $P < 0{\cdot}001$.

For the difference between placebo and amylobarbitone treatment effects, at

90 min, $t_{15} = 3{\cdot}13$, $P < 0{\cdot}01$
and at 180 min, $t_{15} = 3{\cdot}19$, $P < 0{\cdot}01$.

The amylobarbitone induced depression thus developed within 90 min of oral administration and was maintained at about the same level for at least 180 min.

Chlorpromazine (25 and 50 mg) also produced statistically significant depression of the auditory flutter fusion threshold which was greater at 180 min than at 90 min. However, neither 2 mg nor 4 mg of perphenazine altered the auditory flutter fusion threshold, thus distinguishing between the actions of aliphatic and piperazine phenothiazine derivatives.

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