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Circadian Variation in Effects of Ethanol in Man

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LAWRENCE, N. W., M. HERBERT AND W. J. JEFFCOATE. *Circadian variation in effects of ethanol in man.* PHARMACOL BIOCHEM BEHAV **18**: Suppl. 1, 555–558, 1983.—Twenty normal male volunteers received an intoxicating dose of oral ethanol (2 ml/kg vodka) and impairment of psychological functioning was documented over the succeeding 90 min. Half the subjects received ethanol at 0900 hr and half at 1800 hr. Those who received ethanol in the morning performed worse in tests of reaction time ($p<0.002$) and logical reasoning ($p<0.002$), even though blood alcohol levels were similar in the two groups. It is concluded that there is a circadian rhythm in the effects of ethanol in man.

Ethanol   Circadian rhythm   Pyschological impairment

ATTEMPTS to study either the biochemical or the behavioral actions of ethanol *in vivo* in man are fraught with difficulty, and much of the reported data is conflicting. One possible reason for such discrepancies is the circadian variation which may occur in both the pharmacokinetics and pharmacodynamics of ethanol: most experiments on volunteers are undertaken at 0800–1000 hr but in many cases investigators choose the evening, for social convenience. Hitherto there have been extensive studies of possible circadian variation in the absorption and metabolism of ethanol, but relatively few on circadian change in its effects. We report here the effect of moderate blood alcohol concentrations, achieved at two different times of day, on some aspects of psychological functioning in twenty normal volunteers.

METHOD

Twenty normal males (age 19–23 years) were studied. None were taking any medication and none smoked cigarettes. The usual weekly alcohol consumption of the volunteers are undertaken at 0800–1000 hr, but in many cases in-0–280 g (0–15 pints beer). Each had abstained from alcohol for at least 24 hr and had fasted (water only) for 8 hr. To overcome possible variation in practice effect in the tests employed, each subject was studied only once: ten took ethanol at 0900 hr and ten at 1800 hr. All gave written informed consent to the study.

Ethanol was taken orally over five minutes as 2 ml/kg vodka (37.5% v/v) in an equal volume of fresh orange juice. Blood alcohol concentration was estimated from breath analysis using an Alcolmeter AED1 (Lion Laboratories, Cardiff) at 30 min intervals for 90 min. Changes in psychological functioning were determined using three tests: (1) Mood inventory—visual analogue scale designed to monitor self-perceived incoordination [6]. (2) Four-choice serial reaction time [13]—the subject was required to press specific buttons in response to light signals. Response over a ten minute test period was analysed for mean reaction time, errors and variation in reaction time. (3) Logical reasoning—based on grammatical transformation [2]. In five minutes subjects were required to answer as many questions as possible. Results were analysed for total attempted, and % error.

Each subject underwent a standard practice session on the day before the test. During the study psychological functioning was determined before, and at 30 min intervals after taking ethanol (Fig. 1). Statistical analysis was performed using a 2-tailed Mann-Whitney U-test, with significance set at <0.05.

RESULTS

Blood Alcohol Concentration

Mean blood alcohol concentrations are shown in Fig. 2. There were no significant differences between the two groups.

Self-Perceived Incoordination

All subjects felt less co-ordinated after ethanol. Although

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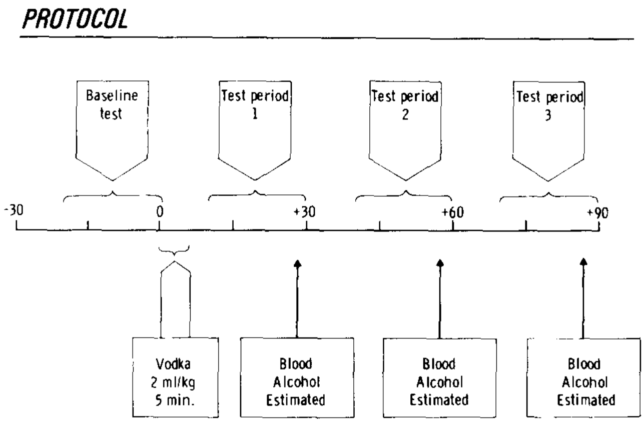

FIG. 1. Protocol for both morning and evening test sessions. During each test period psychological functioning was assessed by Mood Inventory, Four-Choice Serial Reaction Time and Logical Reasoning Tests.

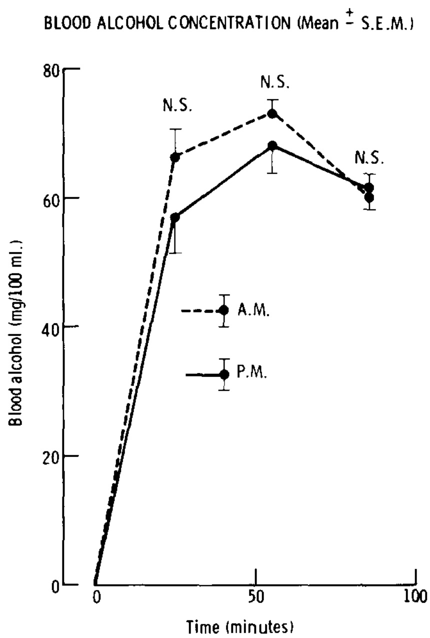

FIG. 2. Blood alcohol levels (mg/100 ml) determined by breath analysis following oral ethanol at 0900 (●---●) or 1800 (●——●), expressed as mean±SEM. N.S., not significant; $p>0.05$. Mann-Whitney U-Test.

this effect tended to be greater in the morning, there was no significant difference between the two groups (Fig. 3).

4-Choice Serial Reaction Time

There was no significant difference between the mean reaction time of the two groups but those studied in the morning made significantly more errors ($p<0.002$ at 55 min; see Fig. 4), and had significantly greater variability in performance—expressed as coefficient of variation of reaction time ($p<0.02$ at 55 min; see Fig. 5).

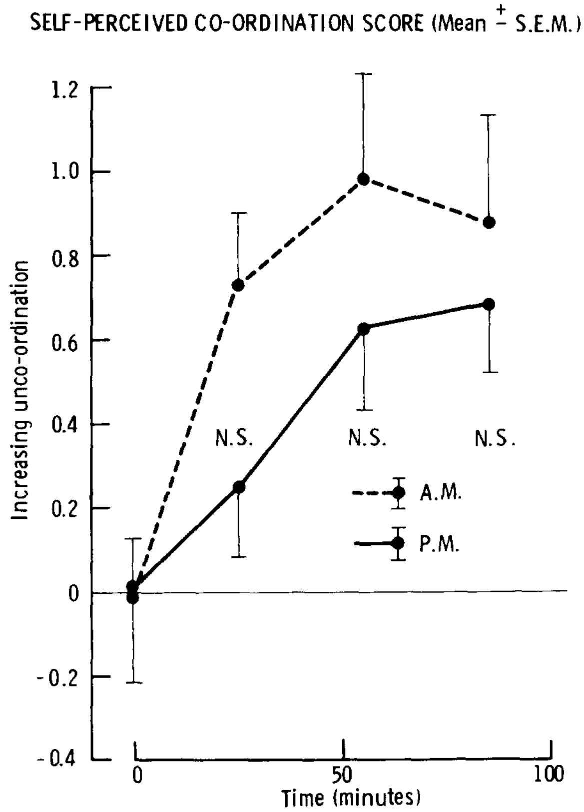

FIG. 3. Deterioration in self-perceived co-ordination score (mean±SEM). ●---●, ethanol given at 0900; ●——●, ethanol given 1800. N.S., $p>0.05$ Mann-Whitney U-Test.

Logical Reasoning

The morning group attempted significantly fewer questions ($p<0.002$ at 25 min; see Fig. 6) but % error was not statistically different between the groups.

DISCUSSION

These results show that the same blood alcohol level is associated with a significantly greater impairment of different aspects of psychological functioning when achieved in the morning, and this confirms the social experience of many who find that drinks taken during the day make one feel more drunk than those taken in the evening. There are a number of possible explanations for this phenomenon.

Some have reported that peak blood alcohol concentrations are higher when ethanol is taken in the morning [8, 9, 14] and that this may relate to variation in the rate of either absorption [9] or clearance [8,14]. The subject has been well reviewed [8, 9, 12]. We, however, found no significant difference between blood alcohol concentrations in the two groups, although the relatively small number of measurements made may have masked minor differences in the rate of rise and fall of blood levels. Since impairment of performance is thought to correlate directly with blood alcohol concentration we conclude that the differences we have found between the two groups must be attributable to circadian change in susceptibility of the body to its effects. Such cir-

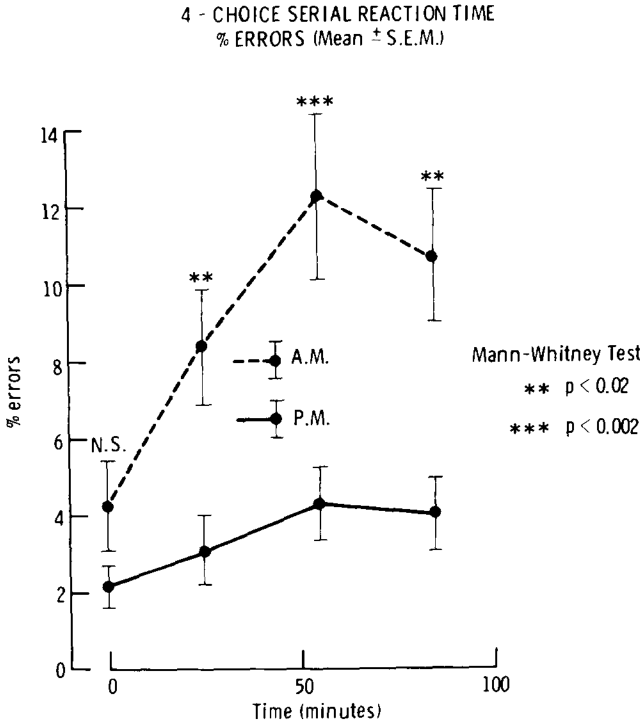

FIG. 4. Change in percentage error in 4-choice serial reaction time test during 80 min following oral ethanol at 0900 (●---●) or 1800 (●——●). Results given as mean±SEM for the ten subjects in each group. $^{**}p<0.02$; $^{***}p<0.002$, Mann-Whitney U-test.

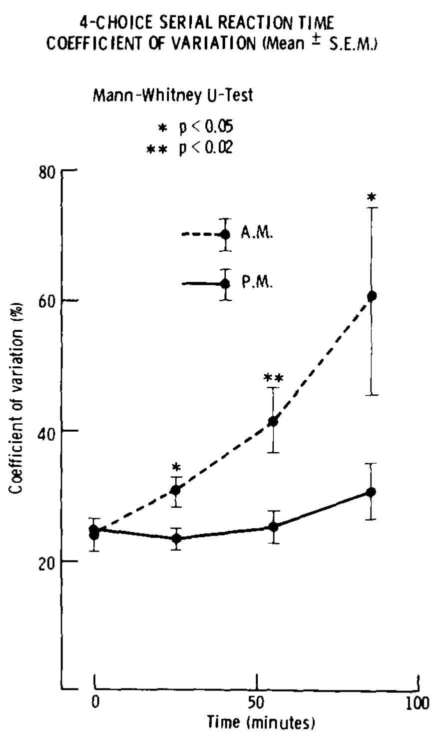

FIG. 5. Change in within-subject coefficient of variation in performance over a ten-minute period in 4-choice serial reaction time test. ●---●, ethanol given at 0900; ●——●, ethanol given at 1800. $^{*}p<0.05$; $^{**}p<0.02$, Mann-Whitney U-test.

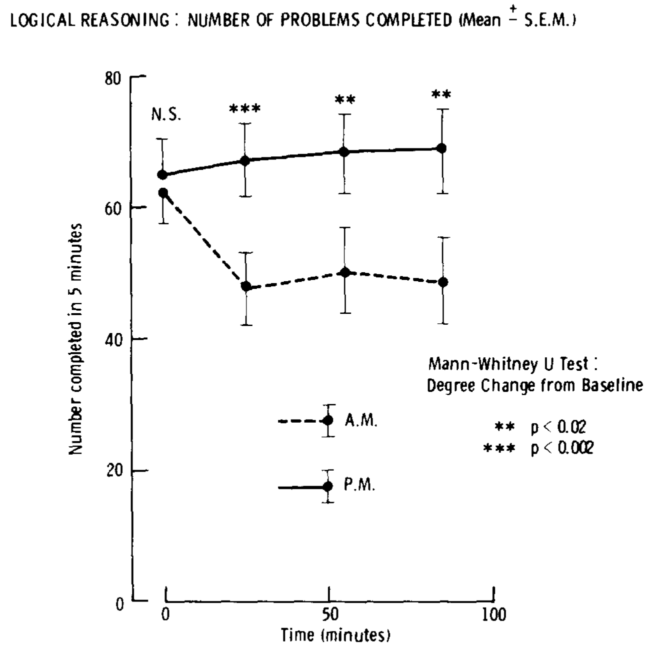

FIG. 6. Logical reasoning test: comparison of number of tasks completed within a five minute test period at different times after ingestion of oral ethanol. ●---●, ethanol taken at 0900; ●——●, ethanol taken at 1600. N.S., non-significant, $p>0.05$; $^{**}p<0.02$; $^{***}p<0.002$, Mann-Whitney U-test.

cadian variation in susceptibility ("chronesthesy") is well known to occur with other drugs [9].

Previous studies on the chronesthesy of ethanol in man have been surprisingly few. Jones [7] has described greater impairment of cognitive performance induced by ethanol in the afternoon as opposed to the evening, while others have reported variation in simple tracking tests [11]. More recently, Minors and Waterhouse [8] have described circadian variation in the diuresis induced by ethanol, with greater urine volumes being passed after morning drinking. It is possible that such circadian changes relate to interaction between ethanol and other body systems in which there is a well established rhythm, and the variation in ethanol-induced diuresis could result from changes in glucocorticoid levels, in antidiuretic hormone or in the renin-angiotensin system. But the existence of such interactions with endocrine or other rhythmic systems remains speculative.

It is also possible that the deleterious effect of ethanol on performance is simply added to the well-recognised inherent circadian variation which occurs in human ability. The work of Akerstedt [1] revealed a lower level of arousal at 0900 than at 1800 hr even though the difference was small compared with overall fluctuations through the day. In two further circadian studies Bjerner *et al.* [3] and Rutenfranz and Colquhoun [10] reported clear "dips" in performance which occurred between 1200 and 1500 hr and between 2400 and 0500 hr. Both groups reported, however, that the scores achieved at the times chosen for the present study (0900 and 1800 hr) were approximately equal, and near-optimal. On the other hand, Blake [4] and Folkard [5] have reported that performance in tasks which require immediate information processing improves steadily throughout the course of the day. Our own results revealed no significant difference between baseline scores of any test in the two groups and therefore tend to suggest that, under the conditions of this experiment, the effect of underlying variability in performance was minimal.

Whatever the mechanism, we have found that the oral administration of ethanol in a dose which achieved blood levels at or below the legal limit for driving in this country, resulted in significantly greater impairment of psychological functioning when taken in the morning as opposed to the evening. This observation has major implications for all who study the behavioural and biochemical effects of ethanol.

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