INTRODUCTION

A long series of joint cross-national studies conducted over the years in our laboratories has been concerned with drug action and interaction on CNS processes involved in road traffic. These studies have ranged from field tests to investigations of underlying CNS functions and the interplay between personality, behaviour, mood, psychophysiological changes and drug levels.

One set of experiments carried out under strictly controlled conditions comparing randomized alcohol and non-alcohol sessions and utilizing a repeated measurement design related to the BAC level aimed at differentiating between the alcohol-induced changes in different phases of alcohol biotransformation on one hand and between spontaneous background activity and stimulus-elicited responses on the other over a wide range of psychophysiological processes: self-rated mood modalities (HOBI et al, 1976), heart rate parameters (MIEST et al, 1977) and electrodermal activity (RICHTER et al, 1977).

In a recent work in this set including a review of the large number of factors influencing CNS effects of alcohol it was shown (SCHWARZ et al, 1980) that alcohol had a triphasic action on EEG background activity parallel to the BAC level, and an inverse biphasic action on stimulus-elicited responses, contrary to the BAC course.
These findings induced us to investigate in detail whether the multiphasic time-courses found for widely different psychophysiological measures were in effect similar in their course and pointed to common underlying mechanisms of action.

The aims of the present work are:
1) to ascertain whether alcohol has uniform excitatory or depressant effects, or differential multiphasic actions related to the BAC level and the phase of alcohol biotransformation;
2) to find possible common underlying CNS mechanisms explaining the wide range of psychophysiological changes observed; and
3) to evaluate the importance of the roles played by the changes in the BAC level and the phase of alcohol biotransformation on one hand, and the differential reactivity of the CNS on the other.

METHODS

Sixteen male policemen used to moderate alcohol consumption served as experimental subjects. The subjects came on a fasting stomach and were given a standard breakfast. The experiments were set up according to a balanced cross-over design, that means each subject was tested on two days, with and without alcohol, the order being randomized between subjects.

<table>
<thead>
<tr>
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<tr>
<td>-17 - 0</td>
<td>Trial 1</td>
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<td>0 - 5</td>
<td>drinking time</td>
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<td>11 - 28</td>
<td>Trial 2</td>
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<td>28</td>
<td>Blood sampling</td>
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<td>39 - 56</td>
<td>Trial 3</td>
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<td>56</td>
<td>Blood sampling</td>
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<td>124 - 141</td>
<td>Trial 4</td>
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<td>141</td>
<td>Blood sampling</td>
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<tr>
<td>239 - 256</td>
<td>Trial 5</td>
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<td>256</td>
<td>Blood sampling</td>
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SCHEDULE OF SESSION

Tab. 1
Five trials were carried out during each experimental session. The first trial served to assess basal, pre-drug values and trials 2 to 5 to assess possible alcohol-induced changes. After each trial the subject had to fill out questionnaires and then blood samples were withdrawn. Each trial consisted in a pre-relaxation period followed by a period of 21 loud tones (sinusoidal tones, 1000 Hz, 100 db, 1 sec duration) terminated by a post-relaxation period. A maximal BAC of one per mil* was attempted, and Vodka was given undiluted (42% v/v) and taken within five minutes. The variables comprised EEG recordings (01/Cz, 02/Cz, ten-twenty system), heart rate, electrodermal activity, mood estimation, self ratings and venous blood alcohol (BAC) determinations.

For the EEG SPECTRAL ANALYSIS a Fast Fourier Transform technique was used with a Hamming window. The frequency domain ranged from 1.25 to 30 Hz in 0.25 Hz steps. Relative and absolute power values as well as the median of the total spectral activity were determined.

Background EEG was defined as the mean of the 21 pre-stimulus epochs each of four seconds duration and the two pre- and post-relaxation epochs.

Stimulus-elicited EEG responses were defined as the 21 differences between the 4-sec post and the 4-sec pre tone epochs. The HEART RATE PARAMETERS were determined from the continuously recorded ECG signal.

Background activity was defined as the 21 mean heart rates over each three seconds before stimulus onset. Stimulus-elicited responses were defined as acceleration (the maximum) and as deceleration (the minimum heart rate) after stimulus onset. The difference between maximal and minimal heart rate denotes the startle reaction to a stimulus.

The ELECTRODERMAL ACTIVITY was measured from the thenar and antithenar of the left palm. A constant current technique was used. The background activity was defined as the frequency of spontaneous fluctuations in the interval between response and onset of the next stimulus. Stimulus elicited responses were defined as a decrease of electrodermal resistance greater than 0.5 kOhm within the first five seconds after stimulus onset; the amplitude was determined.

For MOOD MODALITY ESTIMATION we used a polarity profile with factorized scales based on 20 items. In addition the degree of intoxication and startle reaction were rated on seven point scales.

STATISTICAL METHODS: Means were compared by Student's t-test for dependent samples and in the case of non-normal distribution by the Wilcoxon test. The 0.05 rejection region was adopted in all statistical tests. For the EEG data t-analysis and two Analysis of Variance models were used for comparison to ascertain whether systematic residual effects (carry over) or treatment effects existed; in the models the alcohol and non-alcohol (control) conditions and the two sessions (test-days) were compared. Details are given concerning methods of EEG evaluation (SCHWARZ et

* 1 per mil (o/oo, w/w) = 1 mg per g = 0.948 per mil (w/v) = 0.0948 per cent (o/o, w/v) = 94.8 mg % = 20.6 mM/1.

**RESULTS**

A **BLOOD ALCOHOL CONCENTRATION**

The time course of the venous blood alcohol concentration (fig. 1) is characterized by a rapidly rising absorption phase (trials 2 and 3) reaching a maximum BAC of 0.95 per mil at the 56th minute and a rectilinearly falling elimination phase (trials 4 and 5). At the second and fourth trial a BAC level of 0.75 per mil was found, thus the same BAC in the absorption and elimination phases. Hence we were able to compare effects at two different metabolic phases at the same blood alcohol level. At the fifth trial, the last, almost four hours after alcohol intake, alcohol was still present in the blood, a level of 0.50 per mil being observed.

![Time course of venous blood alcohol concentration.](image)

**B PHYSIOLOGICAL DATA**

The results of the alcohol-induced changes in the physiological data can be divided into two parts, i.e. changes in (1) the spontaneous background activity and (2) in specific stimulus-elicited responses.

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1. Spontaneous background activity

1.1. EEG activity: The alcohol-induced EEG activity was not uniform but showed a biphasic, or even triphasic time course (fig. 2).

![Graph showing EEG activity]

Fig. 2
Alpha activity increased from the initial mean pre-drug level of trial 1 around 45% to a maximum coinciding in time with the BAC peak in trial 3, paralleling the increase in the BAC level during the alcohol absorption phase (trials 2 and 3). Then alpha activity fell in trial 4 even below the pre-drug level, paralleling the fall in the BAC level during the alcohol elimination phase. The alpha activity in trial 5, however, rose, surpassing the initial level.

Alpha and theta activity were closely inversely associated: A rise in alpha corresponded to a fall in theta, and conversely a fall in alpha to a rise in theta, i.e. a time course opposite to that of alpha.

Delta activity varied the same way as theta, hence contrary to the alpha activity and the BAC course.

Beta activity showed a biphasic course similar to that of alpha activity with an increase to a maximum in trial 3 and then a decrease until the last trial, below the initial level. The small fluctuations during the control
session also tended to form a pattern due to diurnal variations, significantly different from that induced by alcohol.

![Time course of the median of total power.](image)

Fig. 3
The median of the total power spectral activity after alcohol intake also showed a triphasic course over time (fig. 3). The median rose from an initial value of 7.5 Hz to a maximum in trial 3, paralleling the rise in BAC, fell in trial 4 parallel to the decrease in BAC and finally rose again in trial 5. - Some fluctuations with time were also observed in the control condition, but less pronounced than the alcohol-induced ones (fig. 3).

The intraindividual variability of the EEG also followed a characteristic time course (fig. 4). Both intra- and interindividual variabilities were high in the pre-drug trial 1 in the two sessions. A clear alcohol-induced reduction was observed in the alpha and theta bands during the absorption phase and a smaller fall also in delta. Parallel to the BAC decrease an increase in variability was observed and then a renewed fall in the last trial. The alcohol induced changes in the standard deviations of these three bands hence displayed the same triphasic pattern as the frequency activities themselves. - The differences from the course in the control session were
obvious (fig. 4).

![Graph of EEG standard deviations with and without alcohol.](image)

**Fig. 4**

1.2. Heart rate: The course showed an increase from the first to the second trial, paralleling the increase in BAC (fig. 5).

![Graph of heart rate with and without alcohol.](image)

**Fig. 5**

However, already at the peak of the blood alcohol curve a decrease in heart rate could be observed until the fourth trial, coinciding in time with the elimination phase, and then a renewed slight increase in the last trial. - The control condition, however, showed a marked
fall during the first four trials and an increase in the last one.

1.3. Electrodermal activity: Here we also observed a triphasic time course (fig. 6):

![Graph showing electrodermal activity](image)

**Fig. 6**

An initial increase, corresponding to the increase in blood level, followed by a decrease already beginning at the peak of the alcohol curve similar to the time course of the heart rate, then decreasing until trial 4 hence following the elimination phase, and finally a renewed increase in the last trial. In the control condition we observed a slow increase throughout the session.

Summarizing all the physiological background changes showed a triphasic course (figs. 2-6) following the BAC, with an initial increase during absorption, a following decrease during elimination and an increase in the last trial at the beginning of the post-alcohol (hangover) phase (GOLDBERG, 1961, 1972).

2. Stimulus-elicited responses

2.1. Stimulus-elicited EEG-changes: By an Analysis of Variance eliminating the fluctuations in the control session we found that alcohol induced significant reductions in alpha, theta and delta responses in trials 2 and 3 i.e. paralleling the increase in blood alcohol (fig. 7).
In trial 4 in the elimination phase the responses increased to the pre-drug level, although they were still smaller in the alcohol condition than in the control session where the responses showed an even higher increase. In trial 5 the responses again showed a reduction.

2.2. **Stimulus elicited heart rate responses:** The difference between maximum and minimum heart rate after stimulus onset, a measure of the startle reaction showed a biphasic time course (fig. 8).
A decrease of the startle reaction was observed in the absorption phase, lasting until the third trial, hence contrary to the increase in BAC, then an increase of the startle reaction in the elimination phase, again contrary to the fall in BAC.

2.3. Stimulus-elicited skin resistance responses (electrodermal activity):

![Time course of the stimulus elicited skin resistance responses.](image)

These responses also showed a biphasic time course with a decrease during the absorption phase, which was larger than in the control session and lasted until the fourth trial in the elimination phase (fig. 9). The following increase in response was delayed in relation to the other physiological responses.

**SELF RATED MOOD MODALITIES**

In the control session only small changes were seen in the self estimated mood modalities as well as a good agreement between the alcohol and the control pre-drug trial 1. The subjects felt relaxed, concentrated and vital, with a marked startle reaction and showed high scores. - Significant and uniform changes, however, were noted in the alcohol session (fig. 10).
With the increase in the blood alcohol level in the absorption phase a marked decrease in all the self-estimated mood modalities was observed. The subjects felt more irritated, less concentrated, less vivid and were less startled by the acoustic stimuli than in the control session. At the beginning of the elimination phase when the alcohol level began to decrease the subjects now showed an increase in the estimated parameters i.e. they felt less irritated, were more concentrated and were more startled than in the absorption phase. At the end of the sessions, in the fifth trial, they estimated themselves about as relaxed, vigilant, and startled as in the control session and with only slightly lower scores than at the beginning of the session.

The time courses of the self estimated mood modalities (fig. 10) hence reflected the biphasic time courses of the stimulus elicited responses (figs. 7-9) with a decrease in the absorption phase and an increase in the elimination phase (fig. 10).

**DISCUSSION**

The repeated measurement design related to the time course of the blood alcohol concentration made it possible to
differentiate the effects of alcohol in the different phases of alcohol biotransformation. Typical examples are the findings at trials 2 (during absorption) and 4 (during elimination) in all measures (figs. 2-10): the two instances showed opposite effects, in spite of the BAC level being the same. - This stresses the necessity when evaluating alcohol effects to take both the BAC level and the course of BAC into account.

Our results have made it clear that all background activity studied (figs. 2-6) followed the same triphasic course, the effects increasing in intensity with the rising BAC level in the absorption phase (fig. 1) and decreasing with the BAC fall in the elimination phase, while all stimulus-elicited responses followed an inverse, biphasic course contrary to that of BAC (figs. 7-9). These results together with the changes observed in self-rated mood modalities (fig. 10), pointed to the possibility that underlying CNS arousal phenomena, i.e. changes in the activation level related to the level of BAC and its course, were likely to explain these seemingly diverse findings.

1. Absorption phase
With regard to spontaneous background activity when taking into account the alcohol-induced increase in EEG alpha and beta activity during the absorption phase, the acceleration of the median frequency (a shift in the median spectral power upwards), the reduction in slow activity in the delta and theta bands, the reduction in EEG variability, the increase in heart rate and in spontaneous skin resistance fluctuations our results infer an alcohol induced excitatory effect on physiological background activity during the alcohol absorption phase, an arousal, i.e. an increase in the activation level, increasing in intensity with rising BAC.

The alcohol induced reduction in specific stimulus-elicited responses in the absorption phase - the reduc-
tion in EEG responsiveness to stimuli with significant reductions in total power and in the alpha, theta and delta bands, together with a decrease in EEG variability, a decrease of the accelerative component of heart rate and of skin resistance reactions also reflects an arousal, an increase in the activation level. Such a view is based inter alia on results from experiments with evoked potentials. In a state of a high degree of alertness, i.e. an arousal or an increase in the activation level, stimulation can evoke reduced potentials, as opposed to the conditions in relaxed wakefulness, fatigue, drowsiness or light sleep when the same stimulus intensity elicits larger potentials, again to be reduced in deep sleep. Hence CNS reactivity is characterized by a bell-shaped response curve with minima at the two extreme ends of the vigilance spectrum, and maxima in the middle region (HERNÁNDEZ-PEÓN et al, 1956, 1957, 1969). The same bell-shaped curve has also been shown to be true for the specific stimulus-elicited responses of electrodermal activity, especially shown in situations of a high degree of activation or arousal, induced by stimulants, emotional stimuli or stressors (COHEN et al, 1956; BURCH & GREINER, 1957, 1958).

It is interesting to see how the subjects themselves perceived the changes in the activation level, as reflected in their self-rated mood modalities. When the BAC rose during the absorption phase the subjects felt increasingly less balanced, less vigilant, less vital and less startled by the acoustic stimuli. The reduction in responsiveness i.e. the decrease of the stimulus elicited responses (figs. 7-9) hence seems to be reflected in the change in the self estimated mood modalities (fig. 10).

Based on these findings we hypothesize that alcohol has acted as a stressor in our motivated police population: in the absorption phase the arousal level increased, accompanied by an increase in CNS background activity
and a decrease in stimulus-elicited responses.

2. Elimination phase
In the elimination phase, with a falling BAC inverse changes were observed: In the background EEG the slow frequencies increased while the fast ones i.e. alpha and beta decreased. The median frequency slowed down and the EEG showed again a greater variability. The frequency of spontaneous skin resistance fluctuations and the heart rate decreased, parallel to the fall in BAC. The stimulus elicited responses, on the other hand, showed an increase. This is also reflected in the course of the self-rated mood modalities: the subjects felt gradually more balanced, more vigilant and vital and became as startled by stimuli as at the beginning of the session.

The fall in the spontaneous background activity and the simultaneous increase of the specific stimulus elicited responses are interpreted as a depressant action of alcohol in the elimination phase parallel to a fall in BAC and a lowering of the activation level.

3. Post-alcohol (hangover) phase
At the last trial in the elimination phase four hours after alcohol intake an increase of various background and stimulus-elicited parameters was observed. These effects are interpreted as excitatory coinciding with the beginning of the post alcohol hangover phase (GOLDBERG 1961, 1972). At this last trial at a BAC level of 0.5 per mil the self estimated mood scores had almost returned to the pre-drug values.

Summarizing our results alcohol-induced effects have been shown to follow a multiphasic course in a number of psychophysiological measures, ranging from mood modalities, EEG and heart rate parameters to electrodermal activity. Spontaneous background activity with a triphasic time-course has followed the BAC level while
stimulus-elicited responses showed an inverse biphasic time-course contrary to the BAC changes.

The underlying CNS mechanisms involve changes in arousal, i.e. in the activation level, leading to differential changes in CNS reactivity, with alcohol acting as a potent stressor eliciting the changes in the activation level; the BAC level as well as the phase of alcohol biotransformation being of fundamental importance for the final effects observed.

Defrayed by grants 6.0490.71 and 6.1080.73 from the Swiss National Fund. Our thanks are due to Jacqueline Kocher for help with preparation of this manuscript.

REFERENCES