INTERACTION BETWEEN ALCOHOL AND TRANQUILIZING AGENTS*

by

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interaction between the effects of alcohol and of CNS-active drugs has been the object of a number of studies in our laboratory. In this series of studies our interest has been devoted to the analysis of the site and mechanism of action of a possible interaction between alcohol and CNS-active drugs by endeavouring to elucidate (1) the role of a possible interference of various drugs with the metabolism of ethanol, (2) the effects in quantitative terms of ethanol and drugs when given alone, and (3) the types of effects of interaction to be induced when alcohol and various substances are combined.

Experiments have been designed which allow following the time course of various effects in relation to blood-alcohol and other parameters; techniques have been developed to detect and record significant departures from normal at low blood-alcohol levels and to allow recording, storage, and evaluation of information suited for quantitative analysis.

The aim of the present communication is:

(1) to study possible relationships between subjective mood estimates, objective performance tests, and blood-alcohol levels;

(2) to analyze the interaction between alcohol and CNS-active drugs with regard to effects on alcohol metabolism, on subjective mood, and on objective behaviour and performance; and

(3) to study whether the interaction found varies with the type of drug investigated and with the phase of ethanol metabolism, whether in the acute phase or in the post-alcohol ("hangover") phase.

Methods

Material: The experimental subjects were healthy volunteers, 20 to 48 years of age, weight 56 to 94 kg, used to moderate alcohol intake. A total of 160 subjects took part in 542 experiments.

Methods: Electro-oculography (EOG): Ocular movements were studied by electrophysiologically recording the displacement of the cornea-retina potentials according to Aschan (1955). For details see Aschan et al 1956 a, b; the actual procedure used and evaluation of the results are given by Goldberg (1961).

Statometry: Standing steadiness, i.e., area of sway while standing, was recorded by transforming the excursions of the centre of gravity, with the subject in a Romberg position on a footplate, via a transducer into a varying voltage. This voltage was fed into (a) a recorder for objective analog recording of the variations in sway, (b) into a frequency analyzer for identifying specific changes in various ranges, (c) into an analog-to-digital converter to a counter and printer for continuous quantitative recording, and (d) on magnetic tape for storage and further feeding into a computer for analysis of specific patterns, quantitative evaluation, and other analyses. Details will be given by Bjerver, Ferguson, Goldberg, Goldschmidt, and Mackay (in preparation).

Psychotechnical tests: The following tests were used: (a) Arithmetic: subtraction of two multiplied figures from a third figure; (b) Spoke A and B: Marking in logical sequence of irregularly placed numbers and/or letters; (c) Reaction time: Apparatus measuring latency time ("lift time") between stimulus and start of response, ballistic time, from start of response to response, and total time (lift + ballistic), in hundredths of seconds.

Subjective mood estimates: Subjective estimation of various mood qualities: from absent-minded and calm to irritated and sleepy, according to a magnitude scale. Normal subjective rating is denoted 10; the subject has to estimate the subjective intensity felt on a certain occasion in relation to a reference standard = 10. Subjective
estimation of degree of intoxication has 0 as starting point. The reference point 10 is defined as being "a little high."


Drugs: Alcohol was given as whisky in a dose of 0.33-0.66 g alcohol per kg. The CNS-active drugs were: amphetamine 10 mg., buclocine 50 mg., chlorcyclizine 50 or 100 mg., chloridiazepoxide 20 mg., chlorpromazine 10 mg., hydroxyzine 25 mg., meclozine 25 or 50 mg., meprobamate 400, 500 or, 800 mg, phenoglycodol 300 mg., promethazine 25 mg., and tripelennamine 50 mg. All drugs were given orally.

Blood-alcohol analysis: Blood samples for analysis were withdrawn in triplicate from a fingertip into Widmark capillaries at fixed intervals, 30-60 min., for a total of 5 to 7 hours; a total of 24-36 analyses were made on each subject.

Ethanol was analyzed by the Widmark micro-method (1932) or by an automated enzymatic ADH-method (Goldberg and Rydberg, 1965). The experimental error of a triplicate sample was ± 0.03 per mil.* The agreement between the two methods was excellent.

Procedure: After one or two initial runs with the whole battery of performance tests and subjective mood estimates to procure a basal value, drugs, or a placebo, and/or alcohol were given on a double-blind basis, coded tablets being used. The battery of tests was repeated at 30 to 60-minute intervals for 5 to 7 hours. In experiments to follow the post-alcohol or hangover phase the tests were repeated for 10 to 12 hours. Each subject took part in several experiments, the order varied on a randomized basis.

Results

A. Effects of Ethanol

Subjective mood estimates: One essential finding was that the time course of intensity of most of the subjective mood variables studied followed closely the same general pattern as that of blood-alcohol. The mood increased in intensity, reached a peak effect about the same time as the blood-alcohol maximum, and subsequently returned to normal, parallel to the fall in blood-alcohol. The subjective estimates were back to normal before blood-alcohol reached zero (Ekman et al, 1963).

Other moods, e.g., "tired," showed, however, a completely different picture. In one of the series the subjects felt very tired even when starting the experiment before the intake of alcohol. After the intake the subjective feeling of tiredness diminished to a minimum, coinciding with the maximum of blood-alcohol. Then the intensity of feeling tired rose again, to show a maximal intensity, even higher than the initial level, at a time when blood-alcohol had fallen or even had reached zero.

The same was also true of "subjective working capacity," showing a maximum at the same time as the "objective working capacity"—of the arithmetic test—was at its minimum and blood-alcohol was at its peak. This experiment thus showed the typical discrepancy between subjective estimate and objective performance occurring after alcohol intake.

A special investigation was carried out to study the possible changes in subjective mood estimates in a "dry run" experiment, i.e., no drug being given, as compared to the changes after alcohol + placebo. In the dry run experiment most moods studied showed a tendency to an "improvement," the subjects feeling less absent-minded, less hazy, less irritated, less sleepy, and less tired. They felt, however, also somewhat less calm and content (Figure 1).

In the placebo + alcohol experiments the results were different. The placebo was given after the initial determination, thus at time—50 min. and the subjects were told that the placebo tablet might have a CNS-active effect. No change was observed in four of the moods—calm, content, sleepy, and tired—but a slight impairment in three—absent-minded, hazy, and irritated (Figure 1).

The administration of alcohol brought about a definite impairment of all moods studied and an increased intensity of those where the placebo had brought about some impairment (Figure 1). The subjects were more absent-minded, irritated, sleepy, and tired and felt more calm and content; the change with regard to irritated was not significant. For those moods where already the placebo had induced some changes—"absent-mindedness" and "haziness"—the changes became more pronounced after alcohol (Figure 1).

Ocular phenomena: Ocular phenomena, especially various forms of nystagmus, have been a matter of interest in this laboratory since 1933.

The introduction of an electrophysiological method to record nystagmus in man by Aschan (1955) made it possible to record, evaluate, and analyze various ocular phe-
Fig. I: Subjective mood estimates. Time course of subjective mood estimates in a dry run and after alcohol + placebo.

--- = dry run
--- = alcohol + placebo

Ordinates: Subjective mood estimates (subj.), starting point 10, changes according to subjective magnitude estimation (see Methods). Subjective intoxication estimate: starting point zero, reference point 10 = "a little high." Blood-alcohol: mg. per ml.

Abscissa: Time axis, from -100 to + 200 minutes. 0 = time of alcohol intake.

The first phase (PAN I) appears about one-half hour after alcohol intake and lasts about 3 to 4 hours after a single dose of alcohol. It is a horizontal, spontaneous positional nystagmus with one fast and one slow component, existing mainly behind closed eyelids in a supine position with the head in lateral positions, beating according to a fixed pattern. With the head in the right lateral position, the fast component is beating to the right, changing its direction with the position of the head and beating to the left in the left lateral position (Figures II, III). PAN I disappears, if of low intensity, when the head is in an upward position or when the eyes are opened.

The second phase (PAN II) appears 5 to 6 hours after intake of a single dose of alcohol and is a horizontal, spontaneous positional nystagmus, also beating according to a fixed pattern but being the reversal of PAN I, i.e., to the left with the head in the right lateral position and changing its direction with the position of the head, beating to the right in the left lateral position (Figure II, III).

PAN II lasts for 5 to 10 hours and in every single case lasts for many hours after alcohol has left the blood (Figure III). PAN II is thus an objectively recorded after-effect. As the latency time, 5 to 6 hours, is constant and independent of dose, this means that after a small alcohol dose PAN II first begins after alcohol has disappeared from the body (Aschan et al, 1956a).

Quantitatively PAN may vary considerably from individual to individual, depending on inherent characteristics of the individual, on environmental influences, on the dose of alcohol, and on the interference of other drugs, e.g., CNS-active drugs in combination with ethanol (Figures VII, VIII).

After moderate doses of alcohol, the frequency of PAN varies between 0.5, and 2 beats per second, the amplitude of a single beat between 2° and 20°. The velocity of the slow phase, corresponding to the inclination in degrees per second of the slow component of a nystagmus beat, varies between 2° and 10° per second.

The best parameters to use as characteristics of the "intensity" of nystagmus are the velocity of the slow component and the area of the time-intensity curve, i.e., (duration in min. × intensity).

With regard to the subjective correlates of PAN it was found that at low intensities, i.e., low amplitudes in the recording, neither...
PAN I or II may be accompanied by any subjective symptoms. Higher intensities however are accompanied by headache, vertigo, dizziness, and even diplopia, nausea, and sometimes vomiting (Aschan et al., 1956a). PAN I and II are elicited in the vestibular system, and the labyrinthine system plays an essential role. When only one labyrinth is functioning, the PAN pattern is changed in a typical way but PAN can still be elicited from either side (Aschan et al., 1964). When both labyrinth are non-functioning, no PAN can be elicited, neither PAN I nor PAN II (Aschan et al., 1964).

PAN II has hitherto been induced in man only, whereas PAN I can be elicited in most experimental animals, even if the mechanism may vary from that of man.

Roving ocular movements (ROM): Roving ocular movements (ROM) are spontaneous horizontal movements of a rhythmic, sinusoidal character, existing mainly behind closed eyelids in a supine as well as in lateral positions of the head (Figure II). ROM usually disappears, when the eyes are open.

The intensity and duration of ROM varies considerably, even in one and the same in-
Fig. III: Positional alcohol nystagmus (PAN) and roving ocular movements (ROM) after alcohol + placebo and alcohol + meprobamate.

Time course and variations in intensity (= ocular movements in degrees per second) of PAN I and PAN II (upper curves), of ROM (middle curves), and of blood-alcohol levels (lower curves), after 0.7 g alcohol per kg.

Left: After alcohol + placebo
Right: After alcohol + 800 mg meprobamate.

Blood-alcohol: 100 mg.% = 1 mg. per ml. = 1 promille (°/oo) = 0.1 per cent (%).

individual on different occasions (Figure III). The frequency varies between 0.2 and 0.5 periods per second, the amplitude between 2° and 25°, and the intensity, i.e., velocity, between 2° and 4° per second (Goldberg, 1961).

ROM may exist before, during, or after alcohol intake; ROM increases when the subject is sleepy or feels tired or after intake of CNS-active agents (Figures III, VII, VIII).

With regard to site of action, ROM most probably is elicited in the reticular system (Goldberg, 1961). Roving ocular movements are accompanied by sleepiness and tiredness. A change in vigilance may bring about a change in the intensity of ROM; concentrating the subject's interest may for some time block the appearance of an existing ROM.

Relationship between PAN, ROM, and dose of alcohol: With regard to PAN, variations in the dose of alcohol—single dose administration—bring about corresponding changes in the intensity of PAN I and II.

If the dose is small and blood-alcohol concentration is below a certain level, usually 0.3-0.4 per ml. (30-40 mg.%), no PAN I or II is induced. With higher doses, the parameters of PAN I and II change in a typical way. With increasing doses, the intensity of PAN I and PAN II, i.e., the velocity of the slow phase in degrees per second and the amplitude increase proportionately; the same is also true of the duration of PAN II.

The times when PAN I begins (= latency of PAN I) and stops, i.e., the duration of PAN I, as well as the time when PAN II begins (= latency of PAN II) are more or less constant and independent of dosage.

With regard to ROM, the intensity of ROM is not, however, in any simple way related to blood-alcohol levels. ROM varies from individual to individual; it varies with time in one and the same individual with
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SUBJ ABS IRR 
V S' CALM SLEEP
CONT/TIREO 
VAA 

m g/ml 
0.8 
0.4 
0
BLOOD-ALC 
8 /
°A 
• /X 
0 
L*L 

m g/ml 
0.8 
280
INTOX -100 0 100 200 
BLOOD-ALC 
0.4 
0
-100 0 100 200 

■■■■■■■ rT~vrw r - alcohol 
* = dry run 
= alcohol + chlordiazepoxide 
= alcohol + meprobamate 

Fig. IV: Subjective mood estimates. Time course in a dry run and after alcohol + placebo, alcohol + chlordiazepoxide, and alcohol + meprobamate. (For details, see Fig. I.)

the degree of vigilance and with many other factors including environmental temperature and humidity (Goldberg, 1961).

As a rule the intensity of ROM is small on administration of alcohol, PAN dominating the picture (Figure III). In some cases, however, a moderate alcohol dose may elicit a clear ROM, with very little or no PAN; in this case sleepiness and tiredness will dominate the subjective symptoms (Goldberg, unpub.).

Not unusual, however, is an increase in ROM activity during the latter part of the blood-alcohol curve or even after alcohol has disappeared from the blood, i.e., as a true and objective after-effect, alternating with a PAN II (Goldberg, 1961).

Relation between PAN and ROM: An analysis of a number of cases was carried out to see whether there exists a correlation between PAN and ROM. An increase in ROM is accompanied by a decrease in PAN (Figures VII, VIII).

Plotting PAN intensity against ROM intensity shows the inverse relationship, the regression line suggesting a hyperbolic course (Figure VII). Transforming both intensities to their logarithms yields a rectilinear relationship (Figure VIII). This seems to be true not only when evaluating different experiments in one and the same individual, i.e., spontaneous changes, but also when evaluating the results from different subjects and when evaluating experiments where the conditions have been modified by various agents, e.g., CNS-depressant drugs (Figures VII, VIII).

Evidence from different types of experiments speaks in favor of the hypothesis that this interaction of an antagonistic nature between ROM and PAN reflects the antagonism between the reticular and the vestibular systems. Experiments to test this hypothesis are in progress.

B. Interaction Between Alcohol and CNS-Active Drugs.

The addition of various drugs to the intake of alcohol may modify the effects of alcohol in several ways. Various mechanisms may be involved. The drugs may affect metabolism and influence the blood-alcohol level or the level of secondary metabolites, e.g., acetaldehyde, or change the permeability of cell membranes or the sensitivity of receptor sites or interact with enzyme mechanisms, transmitter substances, etc., and leave the breakdown of alcohol relatively unaffected

Alcohol + placebo vs. alcohol + CNS-depressant agents: Some antihistaminics with CNS-depressant action—chlorcyclizine, meclizine, and promethazine in therapeutic doses in combination with alcohol—were shown to reduce positional alcohol nystagmus PAN I and II and increase alcohol gaze nystagmus AGN as compared to alcohol alone, neither tripelennamine nor the addition of amphetamine having any modifying effect on PAN (Aschan et al, 1958).

A number of tranquilizing agents—buclizine, chlorpromazine, hydroxyzine, meprobamate, and phenoglycodol in therapeutic doses in combination with alcohol—also reduced PAN I and PAN II to various extents (Goldberg 1961), and increased the intensity of roving ocular movements (ROM). A typical experiment is given in Figure VI,
showing the change after meprobamate. The tranquilizing agents tested, when combined with alcohol, also increased the area of sway while standing and changed the EEG pattern in a typical way, bringing a reduction in alpha frequency and an increase in alpha percentage and in voltage when compared with the effects of alcohol+placebo (Goldberg, 1961, 1963, Goldberg and Chan, unpub.).

Alcohol + placebo vs. alcohol + chlordiazepoxide or meprobamate: In order to study in detail the possible modifying influence of some CNS-active drugs on various effects of alcohol, a set of experiments was started in cooperation with Frankenhäuser, Fröberg, Myrsten, and Neri. The technique involved repeated estimations of subjective moods and of objective performance, including psychotechnical tests, statometry to measure area of sway, and electrooculography to follow ocular movements (PAN and ROM). The time course of the phenomena studied was followed, and all results were referred to blood-alcohol levels. The experiments were extended to comprise a total time of 10 to 12 hours to include possible after-effects during the hangover phase.

The drugs used in combination with alcohol in this series were 20 mg. chlordiazepoxide and 800 mg. meprobamate.

Four series were carried out: a dry run, alcohol + placebo, alcohol + 20 mg. chlordiazepoxide, and alcohol + 800 mg. meprobamate. Eight subjects took part in these experiments, each in four sessions, one on each condition according to a statistically randomized allotment. The whole experiment was carried out on a double-blind basis with coded tablets, the nature of the drugs not being disclosed until after the analysis of the data was concluded. Preliminary results have been reported by Fröberg (1963), Myrsten (1964), and Goldberg (1965).

Blood-alcohol levels: The addition of chlordiazepoxide or meprobamate in the doses used (20 and 800 mg. respectively) did NOT change the course of the blood-alcohol curve and had no effect on absorption, distribution, or disappearance rate of alcohol (Figures V, VI).

Subjective mood estimates: The time course and intensities of the subjective mood estimates are given in Figure IV. It is seen how changes in the subjective mood estimates occurred already during the dry run experiment and how the addition of the placebo, after the first determination and the alcohol, after the second determination, brought about changes that were contrary to those in the dry run. It is further seen from the Figure how the combination of the two drugs and alcohol again changed the picture.

In most moods studied, alcohol + chlordiazepoxide counteracted the effect of alcohol and brought about an effect that was less than that of alcohol + placebo or for some moods even close to the dry run (Figure IV). Alcohol + meprobamate in most instances increased the effects of alcohol, the intensity of the symptoms being higher than that after alcohol + placebo. This difference in action of chlordiazepoxide and meprobamate is clearly seen when evaluating the subjective estimates of degree of intoxication. Chlordiazepoxide reduced or counteracted the subjective symptoms of intoxication, while meprobamate increased them.

Objective performance: In order to get a general picture of the time course of objective performance tests, the results of Arithmetic, Spoke A and B, and reaction time, simple and choice reaction, lift ballistic and total time were transformed to logarithms. The means for each single determination were calculated and plotted against time to obtain the time course. The
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Fig. VI: Subjective estimates (subj. estim), objective performance (obj. tests), and blood-alcohol after 0.7 g alcohol per kg + placebo (alc. + plac), alcohol + 20 mg. chlordiazepoxide (Alc. + CPX), and alcohol + 800 mg. meprobamate (Alc. + MEP). Means of 8 subjects and of 10 different objective performance tests. Mean curve of objective tests is the difference between the results of the actual alcohol experiments and of the dry run experiment (Fig. V).

The general trend of the performance tests is given in Figure V. It is seen how after placebo + alcohol, the impairment began already after the placebo administration and then increased after alcohol intake. The maximal impairment coincided with the peak of the blood-alcohol curve. Then the performance improved, and was back to the initial or pre-alcohol level about 200 to 250 minutes after alcohol intake. Then performance was impaired again, at a time when the blood-alcohol was zero.

The late and distinct impairment is an indication of an after-effect of alcohol, occurring during the hangover period, 8 to 10 hours after intake, after alcohol has left the blood, parallel to subjective symptoms of being tired and sleepy and parallel to the appearance of alcohol positional nystagmus, phase II (PAN II).

The combined effect of alcohol and the drugs tested varied, depending on the type of drug and on the phase of the alcohol effect studied. During the acute phase, the first 3 to 4 hours after intake, the addition of chlordiazepoxide counteracted the effects of alcohol and diminished the degree of impairment observed, both subjectively (Figures IV, VI) and objectively (Figures V, VI). Meprobamate in this phase had a synergistic action with alcohol and increased the effects, both subjectively (Figures IV, VI) and objectively, inducing an increased degree of impairment (Figures V, VI).

During the post-alcohol phase, 8 to 10 hours after alcohol intake and after alcohol had disappeared from the blood, both chlordiazepoxide and meprobamate counteracted the after-effects of alcohol and reduced the degree of impairment, hence improved performance when compared to the performance after alcohol + placebo (Figures V, VI).

The findings with objective performance tests thus corroborated the changes seen in the subjective estimates. It is to be noticed that the three conditions—alcohol + placebo and alcohol + drugs—were carried out double-blind in a random order, eliminating any possible bias on the part of the experimenter or the subject.

Ocular phenomena: The ocular phenomena recorded (PAN and ROM) were also changed after the combination of alcohol + drug as compared to alcohol + placebo and varied with the type of drug studied.

After alcohol + placebo, the typical positional alcohol nystagmus (PAN I + PAN
II) was recorded, PAN I as usual lasting 3 to 4 hours and PAN II lasting for hours after alcohol had left the blood. In some subjects, especially those being very tired when starting the experiment, also roving ocular movements (ROM) of a low intensity were recorded; in these cases the intensity of PAN was proportionally lowered (Figure VII). The correlation between intensity of PAN and of ROM is given in Figures VII, VIII. The figure shows how an increase in ROM corresponds to a decrease in PAN. The hyperbolic course is changed to a rectilinear regression when absolute values were transformed to their logarithms (Figure VIII).

After alcohol + chlordiazepoxide the picture changed. The mean intensity of PAN was reduced (Figure VII). The intensity of ROM was, however, not correspondingly increased but instead reduced (Figure VII).

When PAN was plotted against ROM after transformation to logarithms (Figure VIII), it is seen how the regression line representing the relation between log PAN and log ROM for alcohol + chlordiazepoxide was rectilinear and had the same slope as after alcohol + placebo. The line was, however, depressed and followed a lower course.

After alcohol + meprobamate, the mean intensity of PAN was reduced, more than after alcohol + chlordiazepoxide. The mean intensity of ROM was correspondingly increased (Figures VII, VIII).

When plotting PAN against ROM and transforming to logarithms (Figure VIII), the resulting regression line, representing the relation between log PAN and log ROM, was rectilinear and had the same slope as after alcohol + placebo or alcohol + chlordiazepoxide. It followed, however, a lower course than after alcohol + placebo or after alcohol + chlordiazepoxide.

Thus even with regard to ocular phenomena, chlordiazepoxide and meprobamate showed differential effects when combined with alcohol.

Summary
Experiments on the interaction between alcohol and tranquilizing agents in man have been carried out, comprising a total of 542 experiments in 160 healthy subjects.

The methods used included subjective mood estimates according to a magnitude scale, objective performance tests including reaction time, Arithmetic, Spoke A and B, further EEG, electro-oculographic recordings (EOG) of ocular phenomena-positional alcohol nystagmus (PAN I and PAN II) and roving ocular movements (ROM), and quantitative evaluation of changes in standing steadiness (statometry). Blood-alcohol levels were followed by repeated determinations.

Various doses of different alcoholic beverages were given, with or without the addition of a placebo or eleven CNS-active drugs in therapeutic doses: from amphetamine, buclizene, and chlordiazepoxide to meprobamate, phenoglycodol, and promethazine.

Fig. VII: Relation between positional alcohol nystagmus (PAN) and roving ocular movements (ROM). Individual cases after alcohol + placebo and after alcohol + CNS-active drugs. Individual intensities of PAN (area = duration × intensity), plotted against corresponding intensities of ROM (area = duration × intensity).
Left: After alcohol + placebo
Middle: After alcohol + chlordiazepoxide (CPX)
Right: After alcohol + meprobamate

Fig. VIII: Relation between positional alcohol nystagmus (PAN) and roving ocular movements. Regression lines of relation between PAN and ROM after alcohol + placebo, alcohol + chlordiazepoxide (CPX), and alcohol + meprobamate.
Left: Regression lines, representing intensity of PAN plotted against intensity of ROM. Intensity = area (duration × intensity).
Right: Regression lines, representing log intensity of PAN plotted against log intensity of ROM.
The drugs were given as coded tablets under double-blind conditions and allotted at random.

The whole battery of tests was run before and after the administration of alcohol with or without another drug at 30-to 60-minute intervals for 5 to 7 hours. In experiments to study the post-alcohol (hangover) phase, the time was extended to 10 to 12 hours.

The main results were: (1) Most subjective mood estimates and performance variables, including standing steadiness, followed closely the blood-alcohol curve, peak effects coinciding in time with blood-alcohol maxima, pointing to blood-alcohol being the main factor involved; (2) Some processes, e.g., latency time of positional alcohol nystagmus phase I (PAN I) and of phase II (PAN II) and duration of PAN I were independent of variations in blood-alcohol, pointing to a trigger mechanism of a more complicated nature; (3) Intensity of PAN II and of ROM were dependent among others on the existing state of affairs in the CNS and the interaction between various regions, mainly the vestibular and reticular systems. The extent of the interaction varied among others with the blood-alcohol curve and its course, whether rising or falling; (4) With regard to after-effects, the experiments performed not only showed the existence of PAN II, lasting for hours after alcohol had left the blood, but also an impairment of objective performance in the post-alcohol period when compared to the results of a dry run; (5) The nature of the interaction between alcohol and drug depended among others on the type of drug tested and on the phase of the alcohol metabolism studied.

As examples it may be mentioned that meprobamate when added to alcohol on a double-blind basis increased the effects of alcohol both subjectively and objectively in all functions studied, including both PAN and ROM.

(6) None of the eleven tranquilizing agents tested changed the course of the blood-alcohol curve, the effects seen thus being confined to changes in CNS reactivity.

References