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# RECOVERY FUNCTION AND CLINICAL SYMPTOMATOLOGY IN ACUTE ALCOHOLIZATION AND WITHDRAWAL

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Withdrawal has often been considered a phenomenon which occurs only after the cessation of long-term alcohol intake. The occurrence of withdrawal signs and symptoms upon cessation of alcohol ingestion is evidence of physiological dependence. It has also been postulated by Seevers and Deneau (1964) that physical dependence is characterized by hyperexcitability of the central nervous system. Consequently, we recently undertook to study changes in brain excitability of alcoholics, during alcoholization and withdrawal. We used the recovery function of somatosensory evoked potentials to assess changes in CNS excitability. Our findings (Begleiter, Porjesz and Yerre, in press) demonstrated that an increase of central nervous system excitability results from the cessation of alcohol intake, even after short periods of drinking. The state of hyperexcitability increases as drinking progresses and appears to reach a peak approximately 34 hours subsequent to withdrawal from prolonged alcohol ingestion. Three days after cessation of alcohol intake, our recovery function values return to normal. Our data support the hypothesis that partial withdrawal is manifested by a latent rebound hyperexcitability which occurs subsequent to depression of the central nervous system by alcohol.

In order to evaluate the significance of our physiological findings, we proceeded to examine the relationship between these physiological measures and the clinical indices of withdrawal. The quantitative clinical indices of withdrawal were developed through the evaluation of withdrawal states in several hundred

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alcoholic patients with the subsequent development of highly reliable clinical evaluation scale (Gross et al., 1971; Gross et al., in press). The 30-item quantitative clinical evaluation of withdrawal (Total Severity Assessment, TSA) is quite useful in assessing daily levels of partial and abstinence withdrawal (Gross and Lewis, in press; Gross et al., in press). The TSA has been found to be quite sensitive to differences in duration of drinking (Gross and Lewis, in press) and appears to be related to differences in characteristics of the acute drinking episode prior to hospitalization.

Evidence supporting the construct validity of the TSA has been obtained in connection with studies relating all portions of the TSA to sleep changes (Gross et al., 1972; Gross et al., in press), acetaldehyde and formaldehyde levels (Korol et al., in press) and comparative treatment studies (Gross et al., in press).

In this paper we report our findings on the relationship between the recovery function of somatosensory evoked potentials and the quantitative clinical indices of withdrawal (TSA) obtained in alcoholics during acute alcoholization and withdrawal.

## METHODS

The experiment was performed on four male alcoholics, with a mean age of about 36. All subjects were heavy drinkers for a long period of time who were admitted to the hospital because of drinking problems. They all volunteered to participate in the study after a drying-up period of approximately three weeks.

The recovery function is determined by stimulating the median nerve of the right wrist, with pairs of stimuli separated by varying intervals; the size of the second brain evoked response ($R_2$) compared with the first ($R_1$), indicates the extent to which responsiveness has recovered after a given interval.

A complete description of the recovery function technique and analysis have been previously reported (Shagass, 1972; Begleiter, Porjesz and Yerre, in press).

Subsequent to a drying-up period of three weeks in the hospital, baseline records were obtained on Thursday and Friday mornings. The testing period lasted for approximately three weeks. In order to examine the effects of time on the recovery function, half of our subjects were first subjected to the experimental (alcoholization) run and then after a period of one week were subjected to the control run, for another period of three weeks. The other half of our subjects received the control run first and then the alcoholization run.

Baseline records were obtained on Thursday and Friday of the first week of testing. On Sunday, the patient received a half-dose of alcohol (1.6 g/kg). On Monday, Tuesday, Wednesday and Thursday of the following week, he received a full dose of alcohol (3.2 g/kg). In each instance we studied changes in brain state, 10 hours after the subject had his last drink. On Friday, alcohol was suddenly withdrawn and a recovery function was obtained on Saturday morning. Finally, records were obtained on Monday, Wednesday and Friday of the third week.

The daily administration of the TSA was similar to the recovery function determination. However, the TSA was administered at 6 a.m., before the evoked potential recordings and at 1 p.m. after the evoked response recordings.

## RESULTS

In order to examine the relationship between the recovery function data and the clinical indices, it was necessary to group the recovery function scores for all nine interstimulus intervals used. This enabled us to obtain a quantitative level of CNS excitability for each day of testing. The comparison of our findings for the alcoholization run and the control run are illustrated in Figure 1. The analysis of variance comparing the alcoholization run with the control run yielded an F ratio of 21.73, significant at the $/.01$ level.

Since the TSA was administered before and after the evoked potential recordings, we decided to take a mean score of the TSA. This score was then correlated with our daily recovery function score.

The correlation coefficient between our clinical and physiological measures is .72 and is significant at $/.02$ level. (Figure 2)

## DISCUSSION

Our present data with patients are very consistent with the concept that enhanced brain excitability is a direct result of alcoholization. Furthermore, our observations indicate that the magnitude of hyperexcitability is directly correlated with the severity of withdrawal symptomatology. As intensive drinking progresses, the hyperexcitability increases as do the clinical indices of withdrawal.

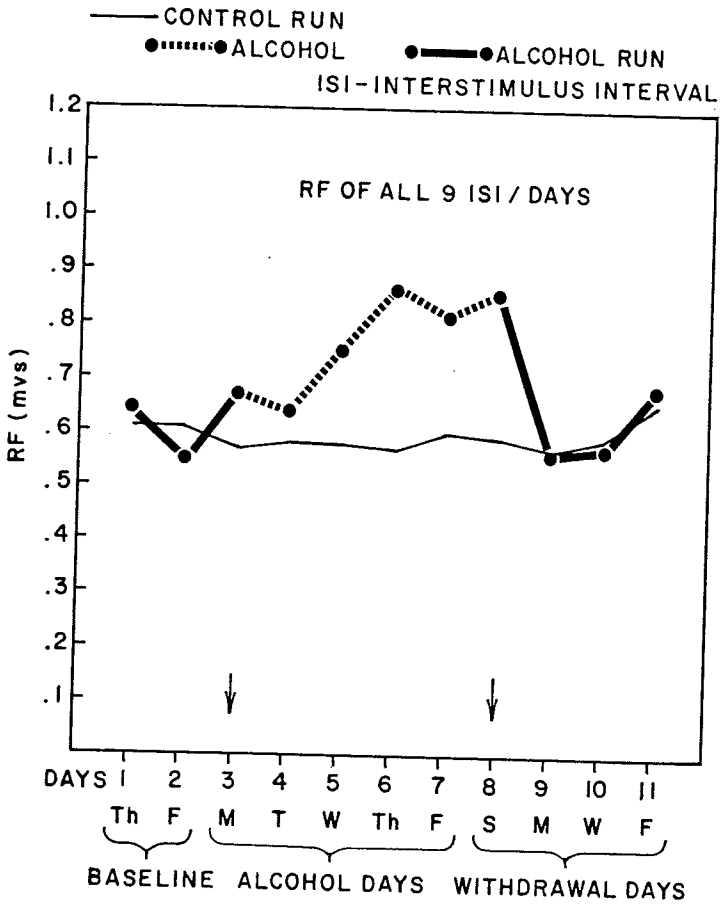


Figure 1

When these scales were applied during the period of alcoholization, it was apparent that withdrawal symptomatology developed after the first day of alcoholization and increased on each subsequent morning, reaching a fairly high level on the fifth day of alcoholization. That these symptoms were primarily symptoms of withdrawal and not intoxification is indicated by the fact that during each day of alcoholization they reached their peak at the period of greatest withdrawal (1 p.m.) and were lowest at the period of maximum alcoholization (10 p.m.).

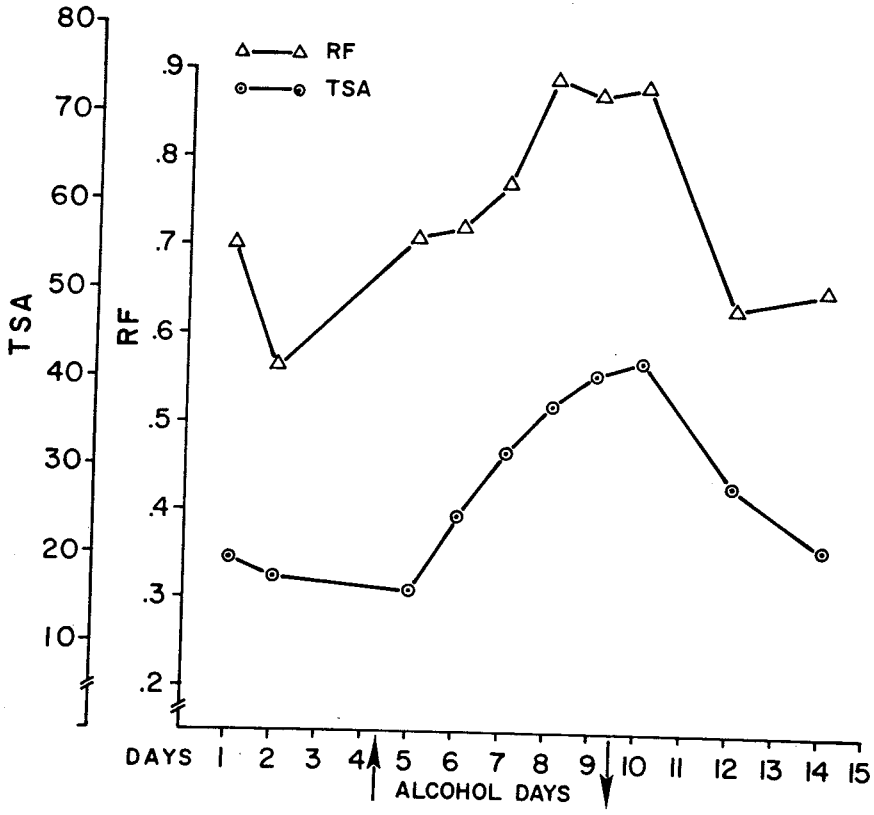
RF
TSA
80
70
60
50
40
30
20
10
.9
.8
.7
.6
.5
.4
.3
.2
DAYS 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
ALCOHOL DAYS

FIGURE 2

Similar results have recently been reported by Goldstein (1972). She found that in mice, the intensity of withdrawal convulsions increased with duration of exposure to alcohol and with blood alcohol levels. Goldstein reported that mild withdrawal signs appeared after a single injection of alcohol. Furthermore, she found that mice could be simultaneously intoxicated and in the early stages of withdrawal.

These data are in keeping with our present findings and are corroborated by recent observations in our laboratory (Begleiter and Standish). We have found that after a single intubated dose of alcohol (6 gm/kg) in rats, there is a marked increase in cortical excitability 10 to 14 hours after alcohol administration. This state of hyperexcitability becomes increasingly more pronounced for each day that alcohol administration continues. We have also observed that in rats, central nervous system hyperexcitability occurred in the early stages of withdrawal, while the animals were still somewhat intoxicated.

At present it is our feeling that the recording of brain evoked potentials is an excellent technique to study changes in central nervous system during alcohol intoxication and withdrawal.

Although the data presented here do not permit us to speculate on the causal relationship between brain hyperexcitability and the increase in the severity of withdrawal symptomatology, our findings do support the hypothesis that the occurrence of withdrawal symptoms is highly correlated with an increase in central nervous system hyperexcitability.

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