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ALCOHOLISM: CLINICAL AND EXPERIMENTAL RESEARCH

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# ALCOHOL AND BRAIN DYSFUNCTION

## Brain Dysfunction and Alcoholism: Problems and Prospects

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Alcoholism is a uniquely human condition. While alcohol intake and alcohol dependence have been successfully induced in a variety of laboratory animals (Ericksson et al., 1980), the complete spectrum of alcoholism with all of its physical, psychological, and social processes can only be found in humans. The clinical manifestations of alcoholism invariably combine the etiological factors and the medical consequences of chronic alcohol abuse.

It is important to note that the brain is the primary target site at which alcohol produces intoxication, dependence, and neurotoxicity. The ingestion of alcohol is well known to result in changes in the central nervous system (CNS). These CNS aberrations are manifested during mild or acute intoxication, during the acute withdrawal episode and the protracted subacute withdrawal period, and finally during the post withdrawal or long term abstinence period.

The acute administration of alcohol results in changes in basic brain processes such as the biophysical properties of membranes (Kalant, 1971; Chin and Goldstein, 1980), neurochemistry (Wallgren and Barry, 1970) and neurophysiology (Klemm et al., 1976; Siggins and Bloom, 1980) and is also evident in complex behavioral processes (Tharp et al., 1974). There are relatively few systematic neurobehavioral studies investigating the long term consequences of chronic alcohol abuse. The clinical and pathological neurobehavioral consequences of chronic alcohol abuse are poorly documented and the pathogenesis remains essentially unknown.

A number of critical issues must be carefully considered in neurobehavioral investigations of brain dysfunction caused by long term alcohol intake.

1. CNS aberrations during acute withdrawal or protracted subacute withdrawal syndrome are frequently accompanied by a cluster of metabolic dysfunctions related to nutritional deficits (Lieber, 1977). These nutritional deficits may in some cases interact with the neurotoxic effects of alcohol to produce irreversible CNS damage (Victor et al., 1971).

2. It is now well established that there exists a subacute withdrawal syndrome which persists long after the acute withdrawal episode has subsided (Walker and Zornetzer, 1974; Porjesz et al., 1976; Begleiter and Porjesz, 1977; 1979; Chu et al., 1978; Begleiter et al., 1980; Bierley et al., 1980). This protracted subacute withdrawal syndrome has been studied in various animals including man and is characterized by hyperexcitability of the central nervous system. The study of CNS dysfunctions caused by the neurotoxic effects of chronic alcohol abuse may be obscured or totally masked by the CNS deficits manifested during the protracted subacute withdrawal syndrome. This problem is particularly critical in the course of investigating possible reversibility or recovery of functions. If the initial assessment of CNS deficits occurs too soon after alcohol withdrawal, the study of reversibility will be confounded by the interaction of withdrawal-related deficits and the neurotoxic deficits caused by chronic alcohol abuse.

3. It is well known that alcohol withdrawal is frequently accompanied by hypomagnesemia and hypophosphatemia (Wolfe et al., 1969;

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Knochel, 1977). Alcoholic patients during withdrawal often manifest respiratory alkalosis which has been shown to significantly reduce cerebral blood flow (Wollman et al., 1968). Consequently, the withdrawal episode may be accompanied by cerebral ischemia which could ostensibly result in persisting brain deficits. These potential long term withdrawal-related deficits should be identified and hopefully differentiated from the CNS deficits caused by the direct or indirect neurotoxic effects of alcohol.

4. The presence of CNS deficits observed in abstinent chronic alcoholics is assumed to be the consequence of many years of alcoholic abuse. There is presently some evidence for the possible role of a genetic factor in alcoholism (Goodwin, 1979). It may be interesting to speculate that the genetic transmission may be expressed by some aberrant functional or structural characteristics of the brain which predispose some individuals to alcoholism. It is imperative to distinguish between those CNS deficits which antedate the development of alcoholism from those which may be the consequence of the disease. The presence of neurobehavioral deficits in chronic alcoholics should not be taken to only reflect the consequence of chronic alcohol abuse.

5. The role of individual differences is important in investigating the effects of chronic alcohol abuse. It is now well established that there are numerous factors, i.e., ethnic background, race, etc., which play a major role in the responses of some individuals to alcohol (Ewing et al., 1974; Reed et al., 1976). It is quite puzzling to understand why, with seemingly identical medical and drinking histories, one alcoholic develops a myriad of CNS deficits while another appears to emerge apparently unscathed. Genetic differences and/or constitutional differences may underlie the individual response of patients to chronic alcohol abuse. The investigation of individual differences in susceptibility to chronic alcohol abuse may contribute to a better understanding of underlying mechanisms.

These are but a few of the critical issues which must be considered in investigating the relationship between alcoholism and brain dysfunction. The aforementioned issues are not specific to any particular discipline, but are basic enough to be relevant to this general area of investigation.

This issue of *Alcoholism: Clinical and Experimental Research* is primarily devoted to the presentation and synthesis of data pertinent to brain dysfunction and alcoholism. Investigators from various disciplines, using different techniques or methods were invited to summarize data and address issues relevant to their respective research areas. Don Walker reviewed the neurohistological, neurophysiological, and behavioral data on the chronic effects of alcohol in animals. These animal studies provide critical information on regional susceptibilities of the brain, as well as shed light on neuropathological mechanisms. The recent development of computerized tomography (CT-scan) has provided the opportunity for examining the brains of alcoholic patients. This noninvasive technique has enabled many investigators throughout the world to study structural changes in the brains of alcoholics. These data are summarized by Lesley Cala. Cerebral ischemia has often been implicated as a possible consequence of chronic alcohol abuse. Consequently, investigators have utilized new techniques to assess cerebral blood flow in chronic alcoholics. These studies are reviewed by Mats Berglund.

The advent of computer technology has led to the development of sophisticated evoked potential techniques used to assess the functional integrity of cortical and subcortical systems. These electrophysiological data reflect various aspects of brain function related to sensory and highly complex integrative processes. Bernice Porjesz has reviewed the electrophysiological findings in alcoholic patients. While clinicians have long been aware of sleep disturbances in alcoholic patients, it is only in recent years that sophisticated sleep EEG studies have been conducted. Harold Williams has summarized the critical literature on sleep EEG in alcoholics. The aforementioned papers deal primarily with the structural and functional characteristics of the brain of alcoholic patients. These various brain processes appear to be aberrant in alcoholics. Therefore, it should not be surprising to learn that the product of these various intricate processes, namely, behavior, is also deficient in alcoholics. Oscar Parsons has critically reviewed the large neuropsychological literature.

The following papers are not meant to provide an all-inclusive and critical account of this vast research area. It is hoped that they will offer but a glimpse of the subtleties and complexities encountered in examining the relationship between alcoholism and brain dysfunction.

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