LETTER TO THE EDITOR

PROPENSITY FOR ALCOHOLISM

To the Editor:

The recent scholarly review of the motivational systems and their relationship to alcoholism (Pihl and Peterson 1995) has inspired me by its sophisticated speculations tying together a multitude of factual data. Two aspects of this erudite exposé happened to resonate with my own musings on the biological underpinnings of ethanol dependence and abuse, namely, the apparent lack of protective effect of alcohol dehydrogenase and the pivotal role of the hippocampus in faulty learning as well as in the vitiated thirst (water regulation) mechanism.

First, the presumably genetic failure of the "inborn Ant-abuse" (Donovan 1986) effect of alcohol dehydrogenase in male European alcoholics (compared with females in general and Asians of both genders) might spare them the aversive impact of the "flushing reaction" of the accumulating acetaldehyde, thus fostering quick progression to higher levels of intoxication. Besides the inherent deficiency of this oxidizing hepatic enzyme in alcoholics (Murray and others 1983), the said noxious metabolite of ethanol might be rapidly removed through further oxidation by the tricarboxylic acid cycle due to the generalized enzymatic induction (Weller and Preskorn 1984). The initial accumulation of acetaldehyde might independently exert a rate-limiting effect on the alcohol dehydrogenase.

Moreover, the alternative neutralization of acetaldehyde through nonenzymatic condensation with monoamines to tetrahydroisoquinolines (Murray and others 1983) may be favored in potential alcoholics by their propensity for anxiety and sympathetic hyperarousal (Pihl and Peterson 1995). These opiate-like alkaloids not only enhance the euphorizing effect of ethanol, but also appear to produce an active craving for it: anything but aversive effects! Intensified craving for alcohol was observed in some depressed alcoholic men (but not women) treated with trimipramine (Kubacki 1981).

Second, the interference with hippocampal function (Pihl and Peterson 1995) could explain the faulty learning whereby the alcoholics learn only too well about the rewarding—anxiolytic and euphorizing—effect of ethanol, but fail to integrate its aversive (punishing) consequences. The affinity of ethanol for hippocampal dendrites and the prefrontal cortex (Lishman 1987) could be responsible for the anterograde amnesia that spares the alcoholics the painful memories of the physical distress and incapacitation as well as the embarrassing or dangerous behavioral antics of severe intoxication. This affinity would also account for their apparent failure to recognize the sensory clues of impending inebriation.

The pivotal position of the hippocampus at the crossroads between the ascending proprio and interoceptive pathways and the networks modulating their alerting, activating, or inhibitory behavioral effects as well as emotional response (anxiety–euphoria or rage versus depression) further elucidates the complex field interaction responsible for the self-destructive habit in terms of maladaptive learning. Its position also ties it to the demonstrated dysfunction of the hypothalamic-pituitary axis (Abou-Saleh and others 1984). The liquid form in which ethanol is ingested implies some interference with thirst (satiation) and water regulation mechanisms, since many alcoholics develop polydipsia and polyuria during periods of abstinence, presumably because of antidiuretic hormone suppression and the resultant diuresis (Ripley and others 1989).

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Andrzej Kubacki, MD, (Med) DSc, FRCPC
Saint John, New Brunswick, Canada