Chronic Alcoholism in the Absence of Wernicke-Korsakoff Syndrome and Cirrhosis Does Not Result in the Loss of Serotonergic Neurons from the Median Raphe Nucleus

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Previous studies have identified alcohol, thiamine deficiency and liver disease as contributing to the neuropathology of alcohol-related brain damage. In order to examine the effects of alcohol toxicity and thiamine deficiency on serotonergic neurons in the median raphe nucleus (MnR), alcoholic and previously published Wernicke-Korsakoff syndrome (WKS) cases without liver disease, were compared with age-matched non-alcoholic controls. While there was no difference between the estimated number of serotonergic neurons in either controls or alcoholics without WKS (means of 63,010±8,900 and 59,560±8,010 respectively), a substantial loss of serotonergic neurons was previously found in WKS cases (mean of 19,050±13,140). Further analysis revealed a significant difference in the maximum daily alcohol consumption between these groups. However, analysis of covariance showed that the number or serotonergic neurons in the MnR did not correlate with the amount of alcohol consumed. Therefore, our results suggest that cell loss in the MnR can be attributed to thiamine deficiency rather than alcohol per se.

Keywords: Alcohol; serotonin; neuropathology; median raphe nucleus; Wernicke-Korsakoff; cirrhosis; thiamine deficiency.

INTRODUCTION

The purpose of this study was to determine the effect of chronic alcohol consumption on the median raphe nucleus (MnR) in a highly selected group of alcoholics without Wernicke-Korsakoff syndrome (WKS) or serious liver disease. The MnR was chosen for...
investigation because in primates (including humans) this nucleus, like the dorsal raphe nucleus (DR), contains a large number of serotonergic neurons (Hornung and Fritschy, 1988; Baker et al., 1991a; 1991b), and together these nuclei comprise the major source of ascending serotonergic projections (Felten and Sladek, 1982). Furthermore, a previous study found substantial neuronal loss from both these nuclei in a single alcoholic case (Halliday et al., 1995). However, this was not substantiated in the DR of carefully selected alcoholic cases without WKS (Baker et al., 1996). Differential sensitivity of the MnR and DR to some neurotoxins such as methylenedioxymphetamine and p-chloroamphetamine has been reported (Mamounas et al., 1991), but it is not known if this is the case with regard to alcohol neurotoxicity.

There is general acceptance that various parameters taken to be indicative of serotonergic function are decreased following chronic alcohol consumption. These include measures of the principal metabolite of serotonin, 5-hydroxyindoleacetic acid (5-HIAA; Ballenger et al., 1979; Tollefson, 1989; George et al., 1992), which is presumed to reflect serotonin turnover. However, a number of factors may have influenced this conclusion. In particular human studies often include alcoholics with WKS or liver disease, making the ascertainment of the effects of alcohol alone difficult or impossible.

This study is an extension of previous investigations measuring the loss of serotonergic neurons from the brainstem of alcoholics with WKS (Halliday et al., 1993; 1995). The present study differs from previous work in that not only alcoholics with cirrhosis, but also those with WKS, have been excluded to assess the effect of alcohol per se on these neurons. The data from this study are compared to data from previously published WKS cases, to examine the role of alcohol consumption in the neurodegeneration of serotonergic MnR neurons in the presence and absence of WKS.

**MATERIALS and METHODS**

The same “control” and “uncomplicated alcoholic” cases were used as described in a previous study of the effect of alcohol on the DR (Baker et al., 1996). The latter cases are hereinafter referred to as “alcoholic cases”. These cases were compared to those described in a previous study of serotonergic neurons in alcoholics with WKS (Halliday et al., 1993), referred to herein as “WKS cases”. Questionnaires to relatives, and telephone interviews with general practitioners were used to obtain information regarding alcohol consumption, diet and mental status (Baker et al., 1996). This information was used as an initial screening procedure to eliminate unsuitable cases. Cases drinking between 20g and 80g of ethanol per day were excluded (see classification criteria below). An attempt was made to select alcoholic cases with equivalent levels of alcohol consumption to that of WKS cases, but all such alcoholics had either WKS or cirrhosis of the liver. For inclusion in this study all cases were required to meet the following criteria: a postmortem delay of less than 72 hours (to ensure viability of relevant enzymes; Törk et al., 1992), no serious liver pathology, and no neuropathological abnormalities other than WKS (Halliday et al., 1993; Baker et al., 1996). For the present study, a number of sections were taken from