

ing glia and vasculature could account for the smaller sulci noted upon further abstinence among these alcoholics, the error in measuring the sulci would seem to be a much more likely explanation. Further, Carlen and colleagues speculate that axonal sprouting and regrowth of supporting glia and vasculature may be responsible for improved neuropsychological functioning observed in alcoholics who remain abstinent. However, synaptogenesis following deafferentation is not always an adaptive response leading to functional improvement as these authors suggest. In at least one study (6) synaptogenesis following deafferentation did not represent recovery from the originally placed dorsal column lesions; upon recovery, mapping of the receptive fields of cells in the thalamus and cortex revealed that information from the front paws of the rat were then channeled into a system presumably specialized to handle hindlimb information, a clearly maladaptive response.

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Hill and Mikhael raise some interesting criticisms of our report of partly reversible cerebral atrophy in recently abstinent chronic alcoholics (1). We respond to their criticisms in order of appearance in their comment.

1) We argue that statistical analysis of the small data set (six abstinent and two drinking patients) is not appropriate. The scans were assessed visually for atrophy by experienced neuroradiologists. The quantification of the atrophy was consistent with the judgments made. The published pictures speak for themselves. Even if the cerebral atrophy was not excessive for the patient's age, the important point was the apparent decrease in the observed atrophy with abstinence.

2) We have compared alcoholics'

scans with those of nonalcoholic, nondemented neurological controls (2, 3). Over the age range sampled (25 to 65 years), most but not all alcoholics had larger ventricles and sulci than the control sample. There was a highly significant separation of the mean scores for each age decade in comparisons of alcoholics to nonalcoholics.

3) Our measurement technique is crude but reliable. The interrater reliabilities of the measures used to score 30 scans was .83 (ventricles) and .93 (sulci). Penn *et al.* (4) have computed ventricular volume as measured from computed tomography (CT) scans using an interactive computer system. They showed that measures of cerebral atrophy of Huckman *et al.* (5), which we used in a modified form, correlate well with larger ventricular volumes but are less precise at smaller volumes.

4) Hill and Mikhael noted only one abnormal scan in the 15 alcoholics they examined. They did not measure cerebral sulci. Their sample was younger than ours and not apparently impaired. Our subjects (1) all showed functional impairment, but none had clinically evident liver disease. Many others have noted cerebral atrophy in alcoholics by use of either pneumoencephalograms (6) or CT scans (7).

5) We agree that the correlation of neuroradiological and neuropsychological data is the procedure of choice in this research. We are pursuing such research (2, 3).

6) Hill and Mikhael argue that measurement error may have accounted for the observed changes. In view of the interrater reliability and the clinical impressions from viewing the scans themselves, we doubt that this is true. As can be seen in figure 1 of our report (1), the visible sulci are remarkably large. More recent, unpublished data from our laboratory and that of R. D. Penn reinforce our earlier conclusions.

7) The biological mechanism of partially reversible cerebral atrophy is unknown. The neuronal deafferentation hypothesis that we suggested related to diffuse ethanol-induced inhibition of protein synthesis, rather than to remote axonal lesions as were used in the study quoted by Hill and Mikhael (8). We know of no cerebral volume or density changes that could be expected from generalized axonal sprouting and synaptogenesis. If regenerative processes were occurring over the whole brain and not in one specific deafferented segment, we see no reason why the brain volume changes measured by CT scans could not occur, particularly if these regenerative

changes were accompanied by glial or vascular growth. We have found a significant cerebrospinal fluid acidosis in recently abstinent alcoholics, which subsides over a period of weeks with maintained abstinence (9). This makes us reconsider other explanations, particularly water and electrolyte shifts, suggested by Heinz *et al.* (10) to explain reversible cerebral atrophy in treated anorexia nervosa. However, the initial results of Penn and Yasnoff (11) showing increased cerebral density on repeated CT scans are consistent with an increase in tissue (particularly protein). Treatment of rats with large doses of ethanol inhibits protein synthesis in the central nervous system, and removal of ethanol reverses this process (12). We hope that our finding of partially reversible cerebral atrophy in adults will continue to stimulate further comments, criticisms, and research.

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