ies. Rats were tested always at the same time each day, in closed, sound-insulated chambers, with continuous white masking noise. There were thus no distractions to interfere with the performance of the task. Another feature that may have influenced the result is that the rat's first response in the session was usually reinforced.

Contrast effect may have contributed to the widespread impression that BSR results in rapid extinction. After watching a rat respond at 100 per minute an experimenter may regard a rate of 5 per minute as extinction, which it clearly is not. Suboptimal electrode placement or parameters of stimulation may account for other failures to achieve good BSR with lean schedules. Sidman *et al.* (*4*), for example, used septal and caudate electrodes.

Our results do not necessarily imply that chaining of responses would not produce further improvement. As pointed out by Cantor, however, most of the reported chaining experiments are confounded by presentation of multiple BSR's at the end of each chain. Cantor's own experiment, which he now claims to be an example of chaining, uses only single BSR's, but, in common with others he has presented no data from unchained control experiments. It may be that such a control is impossible. On any intermittent schedule of reinforcement the unreinforced responses are links in a chain leading to the reinforced response. This applies even to the data of Sidman *et al.* (*4*), the primary source of the belief that performance on lean schedules is impossible with BSR.

The most obvious difference between food reinforcement and BSR is not in degree of chaining but in the fact that food-deprived animals have a mechanism for motivating food-getting behavior while there is no such clearly recognizable motivation for BSR. In a deprived animal expectation of food is readily aroused because it is already being facilitated by hunger. At the beginning of a session, expectation of BSR should be more comparable to expectation of food in a satiated animal. Satiated animals will initiate responding for food (*4*) but quickly discover that food is no longer reinforcing and stop responding. An animal initiating responses for BSR, on the other hand, will have its expectation of reward confirmed and will continue to respond. In fact, it will probably do so with increased vigor because the association of BSR with the situational cues benefits from a recency effect.

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Computed Tomography Scans of Alcoholics: Cerebral Atrophy?

Carlen *et al.* (*1*) have provided us with a stimulating bit of evidence for reversible cerebral atrophy among four of eight alcoholic patients. However, many questions can be raised about their data whose answers would provide an altogether different conclusion.

Reversible atrophy was reported to have occurred only in those patients who remained abstinent from the time the first scan was obtained until the second scan was completed. However, we performed statistical analyses (Student's *t*-test, paired comparisons) of their data and found that the size of the ventricles was not significantly different when measured at an average of about 1 month after the last drink (scan 1) than at an average of about 1 year's abstinence (scan 2). Second, since the authors did not present data for a nonalcoholic control group it is impossible to determine if the ventricular size noted was abnormal even on the first scan. Also, a nonalcoholic control group was not measured twice so we do not know if their computed tomography (CT) method was reliable.

We recently completed a study of 15 alcoholics using CT scans and psychological test performance as indicators of brain pathology (*2*). We found only one case in 15 that was clearly abnormal, even though our subjects had been heavy consumers of alcohol for an average of 15 years. Before it may be concluded that brain damage is reversible upon repeated scanning, as Carlen *et al.* did, it must first be demonstrated that the scans are abnormal initially. From our own findings, we would expect at most only one of these alcoholics to have had abnormal scans upon initial scanning, if they were randomly selected. Other factors such as liver pathology (*3*) and selection of patients because of persistent neurological deficits warranting CT scans on clinical grounds (*4*) greatly increase the number of alcoholics having abnormal scans.

Morphological changes may not correlate with functional changes. For instance, we found many deficits in neuropsychological functioning among our alcoholics who had been abstinent for an average of 1 year, even when the CT scan was normal. Extensive neuronal loss within a circumscribed area must be sustained by the brain in order to detect structural changes by CT scans. Extensive neurophysiological and biochemical alterations can occur among individuals with scans that appear normal, while abnormal scans occasionally are seen among asymptomatic individuals. The combined use of both neuropsychological assessments and CT scans would appear to provide the best estimate of brain pathology.

While Carlen *et al.* noted smaller sulci in repeated scans in some of their abstinent alcoholics, we believe the most likely explanation is measurement error. The authors have stated that the average sulcus measured 1 mm with a measurement error of ± 0.25 mm. We have noted, however, that measurement from the Polaroid print, as done by Carlen and colleagues, introduces around a 3.6-fold increase in the error of measurement because of minification of the print (*5*). This means the average error would be 1 mm, or as large as the average sulcus.

We (*2, 5*) have used the computer printout from the scanner for each slice to determine the total area of the ventricles, sulci, and inner table of the brain. The perimeters can be traced with a transparency and accurately measured with a hand planimeter. From these measurements the ventricle/brain index can be calculated. The advantage of this method is that a volumetric assessment of the ventricles can be made that is relatively independent of the particular cut taken, and the varying size of the brain table can be taken into account. Also, measurement of small structures such as sulci can be accurately determined without a large minification error.

While Carlen *et al.* speculate the axonal sprouting and regrowth of support-

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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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