tality. In contrast, acridine orange reduces cell motility and causes lysis in a few minutes.

Cells stained with FBII show a strong blue and azure fluorescence, which is intense around the nucleus in interphasic cells and very intense in most of the cytoplasm in mitotic cells. Cells stained with FBI show a strong green fluorescence with a distribution in interphasic and mitotic cells similar to the distribution of the blue fluorescence.

Figure 3 shows asynchronous Chinese hamster ovary (CHO) cells stained with FBII. Although the nuclei generally appear relatively unstained, in some nuclei weak fluorescence is apparent toward the center. Cells in or near division are more intensely stained, suggesting that the rounding of these cells places more hydrophobic regions near the surface. Fetal human lung fibroblasts (IMR 90) stained with FBII are shown in Fig. 4. In these cells the fluorescence is brightest around the nucleus in the Golgi area and the nucleus appears unstained. In the mitotic cells most of the cytoplasm is brightly stained but, again, the fluorescence is more concentrated around the nucleus.

Figure 5 shows synchronized S-phase CHO cells stained with FBI. Particularly striking are the fluorescent spots at the nuclear poles, suggesting that cytoskeletal protein in the centrioles has a high affinity for FBI. Rat skin fibroblasts (FR3T3) stained with FBI are shown in Fig. 6. The brightly fluorescent mitotic cells are clearly visible, and the interphasic cells show brighter fluorescence in the perinuclear areas than in the rest of the cytoplasm.

Cells removed from patients with so-called lysosomal disorders and stained with FBI show unique staining properties reflecting abnormal lysosomal patterns. As an example, cultured human fibroblasts from a β-glucuronidase–deficient patient (GM121) stained with FBI are shown in Fig. 7. Cytoplasmic fluorescent particles (lysosomes?) are evident which are much larger and more numerous than those seen in fibroblasts from normal individuals. The area of the Golgi apparatus, which shows brighter fluorescence than the rest of the cytoplasm, does not contain such particles.

Certain proteins can be easily stained by FluoroBora–Carrier buffer systems or ChromoBora–Carrier buffer systems. For example, serum albumin can be treated with dimethylaminonaptho-azomethoxyphenylsulfamidophenyl - 3 - boronic acid or *p*-dimethylaminophenylazophenylthioureidophenyl-3-boronic acid in TAPSO at *p*H 9.0. At this *p*H, much more of the highly insoluble ChromoBoras can be solubilized by TAPSO. As the ChromoBora rapidly enters hydrophobic zones of serum albumin, a short reaction period is followed by dialysis against TAPSO at lower *p*H. The dialysis gradually removes excess ChromoBora without allowing its precipitation from solution, leaving intensely stained protein that cannot be destained except by organic solvents. A protein such as elastin, which is insoluble and highly hydrophobic, can easily be stained by a variety of fluorescent or colored Boradept complexes. The properties of elastin can be employed to prepare a substrate for elastase and other proteolytic enzymes and also to detect elastin in tissue sections (Fig. 8).

Not only insoluble fluorophores and chromophores can be carried into living cells and across the blood-brain barrier by Boradeption, but also modified insoluble drugs, enzyme substrates, heavy metal organic compounds, haptens, and radioactive agents. Past attempts to design effective boron-containing antitumor agents for neutron-capture therapy (*5*) which, on slow neutron bombardment of the boron, release ionizing alpha particles into the tumor with high efficiency, have been relatively unsuccessful. In part, the failures resulted from the limited solubility of most organic boron compounds. These compounds might be taken up by tumor cells if they could be delivered to tissues under physiological conditions. Perhaps this potentially important area of tumor pharmacology should be reexamined in light of some of the present observations.

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2. We refer to this compound as darpsylchloride (diarylpyrazolinesulfonyl chloride). Darpsylchloride can be made soluble in water by the use of cyclodextrin in a manner similar to that used for dansylation of proteins [T. Kinoshita, F. Iinuma, A. Tsuji, *Anal. Biochem.* **61**, 632 (1974); ——, *ibid.* **66**, 104 (1975)]. Darpsylation of immunoglobins at *p*H 8.5 can be used to prepare blue fluorescent antibodies that can be distinguished from, and thus employed along with, fluorescein- and rhodamine-labeled antibodies.
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5. We thank A. D. Ezekiel for his generous gift of fluorescent brighteners; G. Dreyfuss, P. Hauschka, and S. Latt for helpful discussions and advice; A. Broseghini for initial support; and K. Pearson and J. Brill for expert technical assistance. This work supported in part by NIH grants AG-00376-07 and HL-20764-04A1 and by special funds from Children's Hospital Medical Center, Boston.

5 February 1982; revised 1 March 1982

Controlled Drinking by Alcoholics? New Findings and a Reevaluation of a Major Affirmative Study

Abstract. *Controlled drinking has recently become a controversial alternative to abstinence as an appropriate treatment goal for alcoholics. In this study we reexamine the evidence underlying a widely cited report by Sobell and Sobell of successful controlled drinking by a substantial proportion of* gamma *(physically dependent) alcoholic subjects in a behavior therapy experiment. A review of the evidence, including official records and new interviews, reveals that most subjects trained to do controlled drinking failed from the outset to drink safely. The majority were rehospitalized for alcoholism treatment within a year after their discharge from the research project. A 10-year follow-up (extended through 1981) of the original 20 experimental subjects shows that only one, who apparently had not experienced physical withdrawal symptoms, maintained a pattern of controlled drinking; eight continued to drink excessively—regularly or intermittently—despite repeated damaging consequences; six abandoned their efforts to engage in controlled drinking and became abstinent; four died from alcohol-related causes; and one, certified about a year after discharge from the research project as gravely disabled because of drinking, was missing.*

Conventional wisdom in the health professions has long held that persons who have become physically dependent on alcohol must be advised to abstain completely. In 1962, Davies sparked debate by reporting that 7 of 93 alcoholic patients were found on long-term follow-up to be able to drink moderately (*1*). Since then, the controversy has been intensified by conclusions of other investigators that some alcoholics can safely resume social, moderate, or controlled drinking as an alternative to abstinence (*2, 3*).

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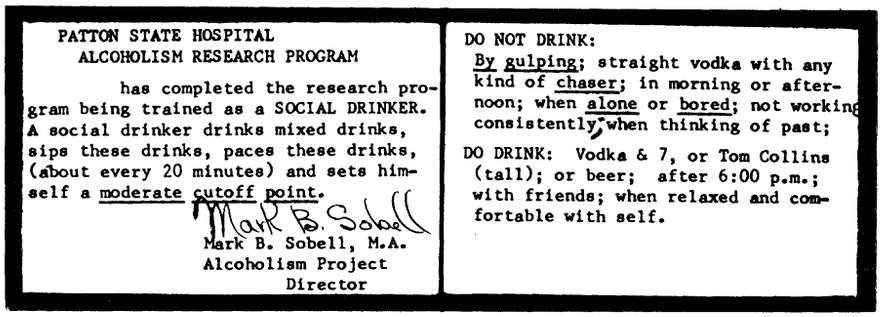

Fig. 1. Photograph of one of the wallet-sized cards (name deleted) given to all controlled drinking subjects when they were discharged from the research project. The back of the card (right) contains individualized drinking instructions. This card was given to subject CD-E 3.

In particular, success has been reported by Sobell and Sobell (*3–7*) with a selected group of *gamma* alcoholics who were trained to practice controlled drinking as part of an experimental treatment program conducted at Patton State Hospital, in California, in 1970 and 1971. This group was reported to have functioned significantly better throughout a 2-year follow-up period than a control group that had been treated with the traditional goal of abstinence (*7*, p. 198). An additional third year of follow-up by Caddy *et al.* (*8*) confirmed the Sobells' conclusions.

Gamma alcoholism, as defined by Jellinek, is characterized by physical dependence with withdrawal symptoms and loss of control (*9*). Of all forms of alcohol problems, it produces the greatest damage. A new and effective treatment would accordingly have great medical and social value and might also call into question basic concepts regarding the nature of alcoholism.

The Sobells' findings have been published in a series of articles and books (*3–7, 10–13*) and are widely quoted (*14–16*). The study was welcomed as a breakthrough, particularly among behavioral and social scientists (*16*), and it seemed to offer a major advance over more traditional approaches that emphasized abstinence.

We have completed an independent clinical follow-up of the Sobells' subjects with the cooperation of Patton State Hospital. Our purpose was to evaluate treatment outcomes and to assess short- and long-term risks and benefits associated with the experimental controlled drinking treatment. Our findings differ greatly from those of the Sobells and of Caddy *et al.* (*8*).

The Sobells' subjects were 40 male alcoholic inpatients at Patton State Hospital (*17*)—all characterized as *gamma* alcoholics—"who requested controlled drinking, had available significant outside support for such behavior, and/or had successfully practiced social drinking at some time in the past" (*5*, p. 54); they were selected by staff decision, on the basis of history and interview criteria (*18*), as appropriate for the controlled drinking goal. The Sobells reported that 20 of these subjects were randomly assigned to an experimental group in which they received behavioral treatment designed to enable them to practice controlled drinking after discharge [controlled drinker–experimental (CD-E) group.] (In this report we refer to these as controlled drinking subjects.) The other 20 were assigned to a control group receiving conventional treatment designed to promote total abstinence after discharge [controlled drinker–control (CD-C)]. (We refer to these as the abstinence subjects.) The Sobells' study compared treatment outcomes of these two groups after discharge.

Controlled drinking subjects received 17 individualized behavior therapy sessions in a simulated bar at the hospital. In the first two sessions, their drunken behavior was videotaped as they were consuming as much as 16 ounces of 86-proof liquor (or its equivalent). The Sobells stated that these sessions further "served to demonstrate to each subject that he could in fact, become quite drunk and then sober up on the next day without suffering from withdrawal symptoms or severe cravings for more alcohol. This information was communicated to the subject in session 3 when the 'myth of one drink' was discussed" (*3*, p. 92; *19*). Session 3 also included "a 'mini-drink' procedure, whereby subjects actually sampled small amounts (1/2 oz) of various types of mixed drinks," based on the assumption that alcoholics have a "gross deficiency in familiarity with mixed [as opposed to straight] drinks" (*3*, pp. 92–93). Sessions 4 through 16 included ten aversion conditioning sessions with electric shock, interspersed with three probe (no shock) sessions. Subjects were shocked for "inappropriate drinking be-

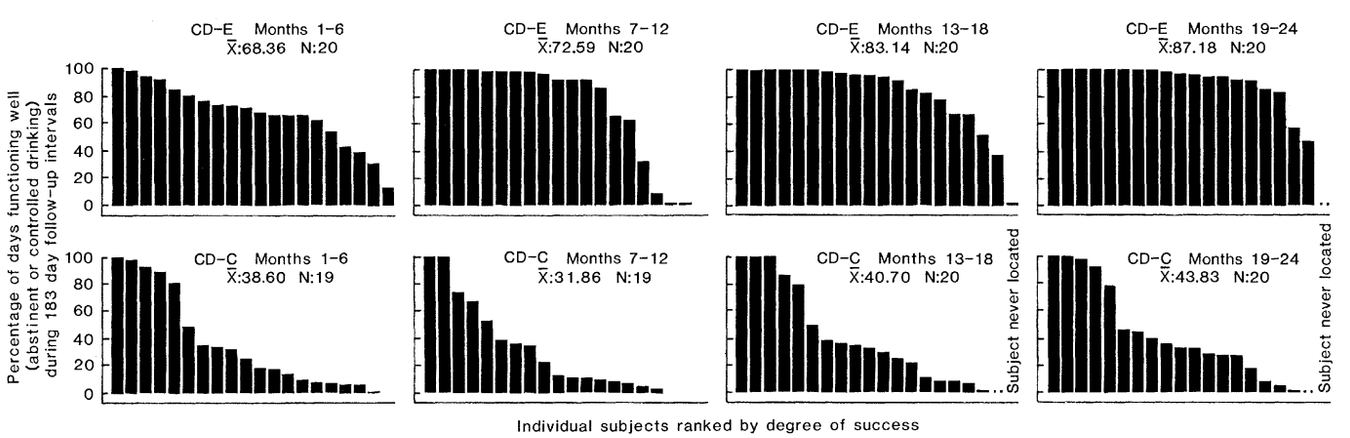

Fig. 2. Percentage of days functioning well (either abstinent or controlled drinking) by individual controlled drinking (CD-E) subjects (upper panels) and individual abstinence (CD-C) subjects (lower panels). Subjects' initials have been deleted from the original figures. Year 1 (left pairs): Reprinted (in slightly modified form) from *Behav. Res. Ther.*, **11**, M. B. Sobell and L. C. Sobell, "Alcoholics treated by individualized behavior therapy: one year treatment outcome," figure 2, Copyright 1973, Pergamon Press, Ltd. Year 2 (right pairs): Reprinted (in slightly modified form) from *Behav. Res. Ther.*, **14**, M. B. Sobell and L. C. Sobell, "Second year treatment outcome of alcoholics treated by individualized behavior therapy: results," figure 1, Copyright 1976, Pergamon Press, Ltd.

haviors" such as ordering a straight drink, drinking more than a prescribed amount in a single sip, or ordering drinks too frequently (*5*, p. 56). Sessions 4 and 5 also had videotape replays to confront the subjects with their own drunken behavior. Session 6 was preceded by a simulated failure experience and focused on subjects' past and present responses to such experiences. Sessions 7 through 16 also provided training in problem-solving, which emphasized "(1) elucidating stimulus controls for heavy drinking, (2) generating a universe of possibly effective alternative responses to those situations, (3) evaluating the probable consequences of exercising each response, and (4) practicing the most beneficial alternative responses under simulated conditions. Thirty minutes of session 16 were videotaped" (*5*, p. 57). In the last (17th) session, videotaped replays of drunken and nondrunken behavior were compared, progress was summarized, and each controlled drinking subject was given a wallet-sized card containing individualized drinking instructions (Fig. 1).

Abstinence subjects reportedly received treatment procedures including "group therapy, chemotherapy, Alcoholics Anonymous, physiotherapy, and other traditional services" (*10*, p. 259). Both groups were followed throughout a 2-year period after discharge.

The Sobells reported both that "Basically, each subject and as many respective 'collateral information sources' as possible were contacted every 3–4 weeks throughout the entire follow-up interval" (*6*, p. 601) and that they relied on official records and collateral sources: "Discrepancies between reports of subjects and collaterals, between reports from different collaterals, or between subjects or collaterals and official records, were always extensively probed, with the final rating being determined by the most objective supporting information available" (*6*, p. 603). Two-year follow-up data were reported for all of the controlled drinking subjects and all but one of the abstinence subjects, constituting "the highest documented follow-up rate in the alcoholism literature" (*3*, p. 118).

The Sobells also reported that during the interviews, subjects and collaterals were asked, "How many days since our last contact have you [has ____, for collaterals] had anything to drink and how much did you [he] drink on each day?" Thus, for each day of a follow-up interval the specific "drinking reported by subjects and CISs [collateral information sources] were recorded verbatim" (*3*, p. 110). Each day was then coded into one of five daily drinking categories (*6*, p. 602): (i) drunk days, defined as "any day during which 10 or more oz of 86-proof liquor or its equivalent in alcohol content were consumed, or any sequence longer than 2 consecutive days when between 7 and 9 oz were consumed on each day" (*20*); (ii) controlled drinking days, defined as "any days during which 6 oz or less of 86-proof liquor or its equivalent in alcohol content were consumed or any isolated 1 or 2 day sequence when between 7 and 9 oz were consumed each day" (*21*); (iii) abstinent days (no alcohol was consumed); (iv) incarcerated days in jail; and (v) incarcerated days in a hospital. This coded daily drinking information constituted the basic data of the study (*22*). The primary measure of treatment outcome was "days functioning well" defined as the sum of abstinent and controlled drinking days, contrasted with days "not functioning well" defined as "the sum of drunk days and days incarcerated in a hospital or jail as a result of drinking" (*7*, p. 198).

Table 1. Order of admission to Patton State Hospital of the 20 controlled drinking and 20 abstinence subjects studied by Sobell and Sobell (*5*).

Date of admission	Controlled drinking subjects	Abstinence subjects
2 April 1970		CD-C 1
28 April	CD-E 1	
1 May	CD-E 2	
2 May	CD-E 3	
4 May	CD-E 4	
5 May		CD-C 2
7 May	CD-E 5	
11 May	CD-E 6	
26 May	CD-E 7	
10 June	CD-E 8	
11 June		CD-C 3
19 June	CD-E 9	
13 July	CD-E 10	
16 July	CD-E 11	
18 July		CD-C 4
27 July	CD-E 12	
1 August	CD-E 13	
23 August	CD-E 14	
28 August*		CD-C 5
28 August*		CD-C 6
2 September	CD-E 15	
11 September*	CD-E 16	
11 September*	CD-E 17	
17 September	CD-E 18	
25 September		CD-C 7
29 September		CD-C 8
14 October		CD-C 9
15 October	CD-E 19	
16 October		CD-C 10
23 October		CD-C 11
30 October		CD-C 12
11 November		CD-C 13
30 November		CD-C 14
29 December		CD-C 15
2 February 1971		CD-C 16
3 February	CD-E 20	
10 February		CD-C 17
18 February		CD-C 18
25 February		CD-C 19
26 February		CD-C 20

*Subjects admitted on the same day are distinguished by the serial number of admission.

The success of the controlled drinking treatment is portrayed in the graphs in Fig. 2 (*6*, p. 606, and *7*, p. 199). Results were reported as percentage of days functioning well. The apparent superiority of the controlled drinking subjects evident in the graphs was significant during each of the follow-up periods (*t*-tests: $P < .005$ for year 1 and $P < .001$ for year 2).

The Sobells referred to alcohol-related incarcerations primarily through tables showing the mean percentage of days spent in hospitals or jails for each group. For instance, during the first 6-month period, they reported that the controlled drinking subjects were incarcerated a mean of 13.09 percent of the days (11.15 percent in hospitals and 1.94 percent in jails) and the abstinence subjects 12.80 percent (3.57 percent in hospitals and 9.23 percent in jails) (*6*, p. 608, table 2). By the fourth 6-month period, however, they reported that the controlled drinking subjects were incarcerated only 1.09 percent of the days (0.46 percent in hospitals and 0.63 percent in jails) and the abstinence subjects 9.44 percent (2.39 percent in hospitals and 7.05 percent in jails) (*7*, p. 200, table 2). Thus, in contrast with the abstinence subjects, the controlled drinking subjects appeared to be improving markedly over the four follow-up periods.

The Sobells concluded: "Controlled drinking, as it was practiced by the subjects of the study, was explicitly not daily drinking; more typically it was a pattern of drinking characterized by one to four drinks on two or three occasions per week to one or two such occasions per month" (*13*, p. 160); "controlled drinking days occurred more often when subjects were at their own residences and in a social context . . ." (*3*, p. 139); and, "subjects who successfully engaged in controlled drinking typically did not initiate extended periods of drunk days as a result of that drinking" (*3*, p. 138).

Caddy *et al.* conducted an independent third-year follow-up (*8*), two objectives of which were "to determine how subjects functioned during their third yr of follow-up," and "to generally determine the validity of the 2-yr follow-up results already reported . . ." (*7*, p. 214). They also reported that the controlled drinking subjects were significantly superior to the abstinence subjects (*t*-test, $P < .03$) (*8*, p. 355), with half of the

Table 2. Controlled drinking experimental (CD-E) subjects rehospitalized for alcoholism treatment within approximately 1 year of their participation in the research project. The time between discharge and first readmission is given in italics, followed by quotations from medical records of their rehospitalizations.

*CD-E 1	*Readmitted to Patton 1 month, 27 days after discharge.* His record states: "Patient is threatening suicide. . . . Diagnosed as a 'paranoid' and 'social drinker' according to the patient. . . . He is brought in by police. . . . He has been drinking but is not totally inebriated."
*CD-E 2	*Readmitted to Patton 1 month, 15 days after discharge.* His record states: First readmission, "returned to drinking wine only was okay one week. . . . Previous stays here have not been too productive." Second readmission, "has developed a tendency to be violent when drinking, getting angry with his wife and has beat her." Third readmission, "has had problems in all aspects of adult functioning. . . . Prognosis—Extremely guarded."
*CD-E 4	*Readmitted to Patton 8 days after discharge.* His record states: "left Patton State Hospital 8 days ago, resumed drinking the next day and now earnestly requests Voluntary Alcoholic readmission. He is tremulous. . . . He is now actively hallucinating, feels he may go into DT's."
*CD-E 6	*Readmitted to Patton 7 months, 9 days after discharge.* His record states: "requests admission as a Voluntary Alcoholic. He states he hasn't had a drink for 1½ days. At present he is extremely agitated and extremely tremulous. . . . He states he sees all 'those G.D. Birds.' . . . admitted for medical care of impending DTs. . . . was averaging one fifth a day."
*CD-E 7	*Readmitted to Patton 3 months, 22 days after discharge.* "requests admission for treatment of alcoholism—was here previously. . . . he thinks he might be close to DT's as he feels confused, sees pictures flash before his eyes and sees little moving objects on the floor. . . . he is grossly tremulous. Denies use of liquor since last night. He has consumed beer and wine over past 3 months."
*CD-E 8	*Readmitted to Patton 13 days after discharge.* His record states: "This . . . intoxicated man is taken in on a 72-hour hold, partly because he is suicidal. . . . This patient was admitted . . . so intoxicated he did not even recall his own name."
*CD-E 9	*Readmitted to Patton 5 months, 11 days after discharge.* His record states: "comes in . . . as a Voluntary Alcoholic, having been here previously last year. . . . He had a quart of beer about 4:00 a.m. this morning. . . . states that he came here because he could not work, his hands were shaking so badly and he was so nervous."
*CD-E 10	*Readmitted to Patton 1 year, 19 days after discharge.* His record states: "transferred to Patton State Hospital . . . on a 14-day Certification . . . as a danger to himself and gravely disabled. . . . Patient was at Patton a year ago on the alcoholic research program. It was the program designed to convert pathological drinkers to social drinkers. Unfortunately it didn't seem to work with him and he had to go on Antabuse to put an end to his excessive drinking." Also, "abandoned the use of his Antabuse about a month ago and began drinking again."
CD-E 11	*Admitted to a Veterans Administration hospital 3 months, 4 days after discharge.* His record states: "diagnosis of Alcoholism. . . . He never drinks socially, just drinks as much as he can get. . . . He states he was drinking 24 hours a day beginning first thing in the morning. . . . He does appear to be depressed, nervous and tense."
CD-E 12	*Admitted to Camarillo State Hospital 8 months, 11 days after discharge.* His record states: "has been drinking off and on since New Year's when he lost his job. He drank heavily for 3 weeks just prior to admission. He has been through Patton's drinking training program. He has been over-dependent on tranquilizers . . . for the past 5 years."
*CD-E 13	*Readmitted to Patton 4 months, 2 days after discharge.* His record states: "Alcoholism, acute. PT been drinking heavily for past 2 weeks. Previously hospitalized for the same problem." "Had near DT's last night." Later: "Now he has lost his job and has had a 502 [charge of driving under the influence of alcohol] and is on probation. . . ." "Had 2 seizures (both in May 1971)."
*CD-E 14	*Readmitted to Patton 8 months, 8 days after discharge.* His record states: "This patient was here . . . and went through the research program that was used at that time and indications were that he might be able to resume social drinking but he realizes now this is a mistake." Patient taken to county hospital 4 months, 16 days after research on a 72-hour hold. His record states: "Above patient is gravely disabled due to excessive drinking."
CD-E 16	*Admitted to Naval Hospital, Camp Pendleton, 4 months, 17 days after discharge.* His record states: "Physical examination at the time of admission revealed a . . . male who was in alcoholic withdrawal. "Habits: alcohol—gallon of wine—white port" Diagnoses included: "Chronic alcoholism, toxic hepatitis."

*Readmitted to Patton State Hospital.

controlled drinking subjects included reported as "functioning well" 100 percent of the days during year 3 (*8*, p. 352, table 2).

In order to assess the results reported for these two shorter-term follow-up studies and to determine the long-term effects of the treatment, we located and interviewed as many as possible of the original subjects. Our initial contacts with the controlled drinking subjects and their collateral information sources were established in the period 1976 to 1979; we have had intermittent contacts with them since that time (*23*). One purpose of these interviews was to locate documentary data (such as records of hospitalizations for alcoholism and arrests for drunk driving) that would confirm or refute the evaluations of the original investigators. These data, supported by affidavits and records of interviews, have led us to conclusions that are very different from the conclusions of the Sobells and of Caddy *et al.*

In reporting our findings, we depart in two respects from the practice of the previous investigators. (i) In place of the subjects' initials, we have used coded numbers (CD-E's 1 to 20 and CD-C's 1 to 20) to maintain confidentiality. Our coded numbers correspond to the subjects' order of admission to the hospital within each group (as determined by their serial number of admission) (Table 1). (ii) Although we studied subjects from both the experimental and control groups, in this report, we focus on the treatment outcomes and long-term experiences of the controlled drinking–experimental group, rather than on comparisons between the groups, for three reasons. First, the Sobells acknowledged the problem of interpretation when control subjects, although directed toward abstinence, were aware that controlled drinking was considered a potentially attainable goal and that they had been selected as appropriate subjects for that goal (*6*, p. 616, and *3*, pp. 164 and 174). Second, the available data suggest that the experimental and control groups may have differed before they were treated. For instance, most of the controlled drinking subjects were admitted to Patton State Hospital earlier than most of the abstinence subjects (Mann-Whitney $U = 82$, $P < .002$). Thus, even were group comparisons appropriate, in our view they could not be made with confidence. Third, we are addressing the question of whether controlled drinking is itself a desirable treatment goal, not the question of whether the patients directed toward that goal fared better or worse than a

control group that all agree fared badly.

Eighteen of the 20 subjects in the controlled drinking group were interviewed. One had died and one could not be located, but their treatment outcomes have also been documented.

The records of Patton State Hospital show that of the 20 controlled drinking subjects, the first 16 consecutive admissions were all appropriately designated *gamma* alcoholics of various levels of severity. (The last four admissions did not have all of the Sobells' specified subject characteristics and are discussed separately.)

Of the first 16, 13 were rehospitalized for alcoholism treatment within approximately 1 year of discharge (Table 2). Ten were readmitted to the alcoholism program at Patton State Hospital, where they had previously received the experimental controlled drinking treatment, and three were readmitted elsewhere (a Veterans Administration hospital in another state, Camarillo State Hospital, and Naval Hospital, Camp Pendleton). The remaining 3 of the first 16 subjects (CD = E's 3, 5, and 15) also had unfavorable outcomes throughout the first 3 years (noted below).

In our view, the references to hospital and jail incarcerations in the Sobells' tables and related discussion do not convey the reality that is evident when the actual incarceration records of each of the controlled drinking subjects are analyzed individually. For example, the Sobells noted that during the first 6 months the controlled drinking subjects were more often incarcerated in hospitals and the abstinence subjects more often in jails, and they said that this difference "might have been the result of voluntary hospitalizations among the experimental subjects, either to curb the start of a binge or to avoid starting drinking at all" (*5*, pp. 65–66). Records such as those reflected in Table 2, together with personal interview accounts of subjects and collaterals, seem to require a different interpretation. The rehospitalizations were not isolated setbacks in persons with otherwise benign controlled drinking outcomes. Rather, they indicated the pattern of serious problems that characterized these subjects' continued attempts to practice social drinking.

Of the 20 controlled drinking subjects, the last four admitted to the study differed somewhat from the first 16. They stated to us that, although they had had alcohol-related arrests, they had not had any prior hospitalizations [one of the characteristics specified for all subjects (*3*, p. 82)] or other treatment for alcohol problems. They also stated that they had not experienced physical withdrawal symptoms prior to entering Patton.

In our view, two of these four (CD-E 17, who had an unfavorable outcome, and CD-E 18, who had a favorable outcome) might have been appropriately designated *alpha* (psychologically dependent rather than physically dependent) alcoholics (*9*). CD-E 17 had had long-standing severe head pain, which he thought was caused by tension. He had jeopardized his job by drinking to deaden the pain. After he was discharged from the research project, his drinking worsened and he lost his job. Later his pain was attributed to compression of cervical nerves, and spinal surgery was performed in January 1973. Surgery left him disabled, but with less pain. He then began to drink moderately much of the time, but continued to become very intoxicated on weekends. Other consequences of his continued heavy drinking, such as incarcerations for multiple alcohol-related arrests, did not occur until later in our long-term follow-up.

CD-E 18, a heavy drinker for some time, had had a personal problem that led to increased drinking in the year prior to his entering Patton. After participating in the experiment and successfully resolving his problem with the help of a Patton psychiatrist, he no longer engaged in episodes of excessive drinking. His wife's statement, his Patton medical record, and his score on the Alcohol Dependence Scale (*24*) are consistent with his self-report that he had not experienced physical withdrawal symptoms. In our evaluation, CD-E 18 was the only one of the 20 subjects who succeeded at controlled drinking.

The remaining two controlled drinking subjects admitted, CD-E's 19 and 20, were referred by the court as a result of

Table 3. Current findings regarding third-year treatment outcomes of the six subjects ranked highest by Caddy *et al.*, all of whom they reported as functioning well 100 percent of the days in that year.

CD-E 1	Subject and multiple collaterals state he drank heavily throughout year 3, during which he resided in three states. He used an assumed name on his driver's license because of an outstanding alcohol-related felony bench warrant issued in year 2. In February, year 3, police were called by neighbors of subject's mother, when he threatened violence and caused a disturbance while drunk, and in April, he was too drunk to attend his brother's funeral. (This trend continued and in year 4 he was arrested for drunk driving and rehospitalized.)
CD-E 5	Subject states that "the third year included some of my worst drinking experiences." In August 1972, "after drinking more than a fifth of liquor per day, I went to the San Bernardino Alcoholism Services for help. I was having shakes and other withdrawal symptoms and was very sick physically. By then, a physician had told me I had alcohol cirrhosis of the liver." A record of the subject's application for treatment there, his wife's statement, documentation of subsequent hospitalization for alcoholism treatment, and continued deterioration of his health are consistent with his self-report.
CD-E 11	Subject and collateral state that year 3 was his worst year. His records show he spent time in jail, in a state hospital, and in a Veterans Administration hospital because of actions he committed while intoxicated. Toward the end of year 3, he had additional arrests, including one for drunk driving.
CD-E 13	Subject and multiple collaterals state that he was abstinent throughout year 3. He states, however, that this was in spite of the controlled drinking treatment. He became abstinent only after additional alcohol-related incarcerations in hospitals, jail, and road camp. He then spent 5 months of year 2 at Twelve Step House, an AA-oriented alcoholism recovery home, to which he attributed his abstinence.
CD-E 15	Subject and multiple collaterals state he was drinking excessively (sometimes as much as a fifth per day and some beer) when he was not going to be at work. (His blood alcohol of 0.34 percent on a recent admission to a hospital confirms his high reported tolerance.) He had not yet experienced serious alcohol withdrawal symptoms during year 3 and did not require hospitalization. According to his family, however, his health was already beginning to deteriorate, leading to repeated alcohol-related medical problems and hospitalizations from 1976 to the present.
CD-E 18	Subject and collateral state that he successfully controlled his drinking throughout year 3, although, "it would not be entirely accurate to say I never drank excessively." We found no evidence of alcohol-related problems in any major life area. In our view this subject, who apparently had not experienced physical withdrawal symptoms, might have been appropriately designated an *alpha* (psychologically dependent) alcoholic (*9*).

alcohol-related arrests. The former had been reported to be a successful controlled drinker and the latter about average for the group (*6–8*). Both continued to engage in intermittent excessive drinking, but neither was arrested again until the latter part of our long-term follow-up. In part because of their lower levels of alcohol dependence, documented consequences of their drinking did not occur until after the initial 3 years.

Our data relating specifically to the controlled drinking subjects' third-year treatment outcomes are very different from those of Caddy *et al.* (*8*). Table 3 presents our third-year findings for the six subjects ranked highest by Caddy *et al.*, all of whom they reported to be functioning well 100 percent of the days. By contrast, we found that four of the six had apparently engaged in excessive drinking that year. Of the two we evaluated as functioning well, one (CD-E 13) had done so only after three additional hospitalizations for alcoholism and incarcerations in jail and road camp for alcohol-related arrests. He then spent 5 months during his second-year follow-up in Twelve Step House, an Alcoholics Anonymous–oriented alcoholism recovery home, to which he attributed his total abstinence.

Caddy *et al.* specifically mentioned two other controlled drinking subjects in the text of their report (*8*, p. 351). They excluded the data of CD-E 6 from the statistical analyses because, although "abstinent," he was "incarcerated throughout the third year." They included the data of CD-E 9, who had "developed Parkinson's disease," because he reported having "used no alcohol during the third year follow-up," although "with special effort he could have obtained and consumed alcohol"; they described him as functioning well 100 percent of the time. Our documented findings regarding these two subjects reveal (i) that, during most of that year, the former was neither incarcerated nor abstinent, but free and drinking heavily, and (ii) that the latter neither had Parkinson's disease (although for a while he pretended to have it, in part to obtain Valium and other medications) nor was abstinent, but drank heavily along with taking the pills. The law enforcement records of the former (showing seven alcohol-related arrests followed by release) and the hospital record of the latter (including emergency room visits) for that year verify their self-reports.

The long-term drinking histories of the 20 controlled drinking subjects throughout the more than 10 years until the end of 1981 (the termination of our follow-up) were consistent with the data we obtained for the first 3 years. That is, the subject who had controlled his drinking after discharge was still doing so in 1981. Similarly, the subjects who had been unable to control their drinking after discharge were either still drinking heavily despite repeated damaging consequences, abstaining completely, or dead.

One controlled drinking subject (CD-E 18) continued to drink throughout the long-term follow-up period without showing symptoms of *gamma* alcoholism. He successfully maintained his pattern of controlled drinking and said his tolerance had eventually decreased to three to four drinks.

Eight controlled drinking subjects (CD-E's 2, 5, 7, 8, 9, 15, 17, and 20) continued to drink excessively—regularly or intermittently—throughout the long-term follow-up. All had one or more of the following verified alcohol-related consequences during the 1979–1981 period: job loss, arrest, marital breakup, and hospitalization for alcoholism and related serious physical illness. For example, CD-E 2 was hospitalized during December 1981 in an alcoholism treatment program, after a marital breakup and job loss as a result of his drinking; CD-E 15 was hospitalized between July 1981 and October 1981 with a brain contusion and severe retrograde amnesia from a fall (blood alcohol on admission, 0.34 percent); and CD-E 20 was arrested in 1979 after a drunk driving accident; in 1981, he consulted an alcoholism program after reaching what he called, "my own version of skid row."

Six controlled drinking subjects were abstaining completely by the end of our follow-up. The four (CD-E's 1, 4, 11, and 13) with the longest continuous abstinence (3.5 to 10 years) all stopped drinking only after multiple rehospitalizations, with their final treatment being strongly oriented toward abstinence. The fifth, CD-E 3, after years of uncontrolled drinking, decided to stop entirely in 1975 and remained abstinent through 1981 except for two or three brief (1- to 3-day) relapses when he "got drunk and went off the deep end" in reaction to serious crises. The sixth, CD-E 19, had completed more than 2 years of continuous abstinence by the end of our follow-up, ever since being hospitalized for a disabling accident sustained during a heavy drinking episode.

Four controlled drinking subjects eventually died alcohol-related deaths: CD-E 6, age 41, was found "floating face down in a lake" (blood alcohol, 0.30 percent) (*25*). CD-E 12, age 40, died of a "massive myocardial infarction" (*26*). The attending physician stated, "I explained the relationship of his dangerous medical condition to his drinking, and . . . [he] abstained from alcohol for approximately the last year of his life. Unfortunately, his abstinence was instituted too late to prevent his untimely death . . ." (*27*). CD-E 14, age 41, died of "Respiratory failure, minutes, due to ethanol intoxication, days" (*28*). CD-E 16, age 60, died of "Suicide: Drowned when jumped from pier into bay" (blood alcohol, 0.30 percent) (*29*).

One controlled drinking subject (CD-E 10) was still missing. His early record (Table 2) shows that he was certified about a year after discharge from the research project as gravely disabled from drinking.

We have deliberately restricted this report to issues relating to treatment outcomes rather than methodology in order not to obscure the critical question: Does the factual, objective evidence support the Sobells' statement that "many of the CD-E subjects engaged in limited, nonproblem drinking throughout the follow-up period" (*3*, p. 155) and their conclusion that training directed toward controlled drinking is an effective therapy for *gamma* alcoholism?

Reports of the Sobells' study have influenced some clinicians, researchers, teachers, and students to believe that controlled drinking is not only feasible for a significant proportion of *gamma* alcoholics, but also for some may even be more attainable and safer than a goal of abstinence.

The results of our independent follow-up of the same subjects, based on official records, affidavits, and interviews, stand in marked contrast to the favorable controlled drinking outcomes reported by the Sobells and Caddy *et al.* Our follow-up revealed no evidence that *gamma* alcoholics had acquired the ability to engage in controlled drinking safely after being treated in the experimental program.

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17. Thirty additional subjects, who did not meet the criteria for the controlled drinking treatment goal, were used in a parallel experiment that compared behavior therapy with conventional therapy when both had total abstinence as a goal. Since the Sobells reported no lasting differences between the two groups in the parallel experiment, we omitted it to simplify the exposition. We followed these patients also but do not report their results here.
18. "Screening factors included a reported minimal history of impulsiveness and past indications of exercise of self-control over other behaviors. . . . The staff also considered various other factors. . . . [such as] subjects having relatively few alcohol-related hospitalizations and arrests, being younger, reporting a shorter history of drinking problems, and having greater educational attainment" (*3*, p. 84).
19. This "myth" refers to the belief that alcoholics "will immediately or eventually proceed to drink to drunkenness should they ingest an initial drink" (*3*, p. 73).
20. For the second-year follow-up, drunk days were defined as "usually consumption of greater than 6 oz of 86-proof liquor or its equivalent in alcohol" (*7*, p. 196).
21. For the second-year follow-up, "usually consumption of 6 oz or less. . . ." (*7*, p. 196).
22. The Sobells also reported additional individual drinking data including the type of beverage, the length of longest binge, and the social environment and location in which drinking typically occurred (*7*, p. 203, table 4).
23. We also followed the 20 abstinence subjects, but less intensively. Eleven subjects and the widows of two others were interviewed. Another had already been reported to have died (*7*, p. 209), and six remain unaccounted for.
24. The alcohol-dependence syndrome is described by G. Edwards and M. Gross [*Br. Med. J.* **1**, 1058 (1976)]. To assess the severity of the syndrome, we have recently begun to use a questionnaire developed by T. R. Stockwell, R. J. Hodgson, G. Edwards, C. Taylor, and H. Rankin [*Br. J. Addict.* **74**, 79 (1979)]. However, since the lowest response category on the original questionnaire is "almost never," we needed the response "never" to discriminate subjects who did not have the syndrome at all from those with low levels of severity. Therefore, for each item, if a subject responded "almost never," we asked, "Which would be the most accurate response, "never" or "almost never"? Subject CD-E 18 obtained a score of zero, having responded "never" to all relevant questions. His responses were confirmed by his wife.
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Hair-Cell Innervation by Spiral Ganglion Cells in Adult Cats

Abstract. *A horseradish peroxidase technique was used to trace the peripheral terminations of two types of ganglion cells in adult cats. It was found that large, usually bipolar ganglion cells end on inner hair cells and small, usually pseudomonopolar ganglion cells end on outer hair cells. Thus, a virtually complete segregation of afferent neural inputs from the two types of hair cells was directly confirmed.*

The cochlea receives sound stimulation and generates activity in fibers of the auditory nerve. Incoming mechanical signals are transduced by sensory cells (hair cells) that lie on the basilar membrane. The typical mammalian cochlea has one row of inner hair cells (IHC's) and three rows of outer hair cells

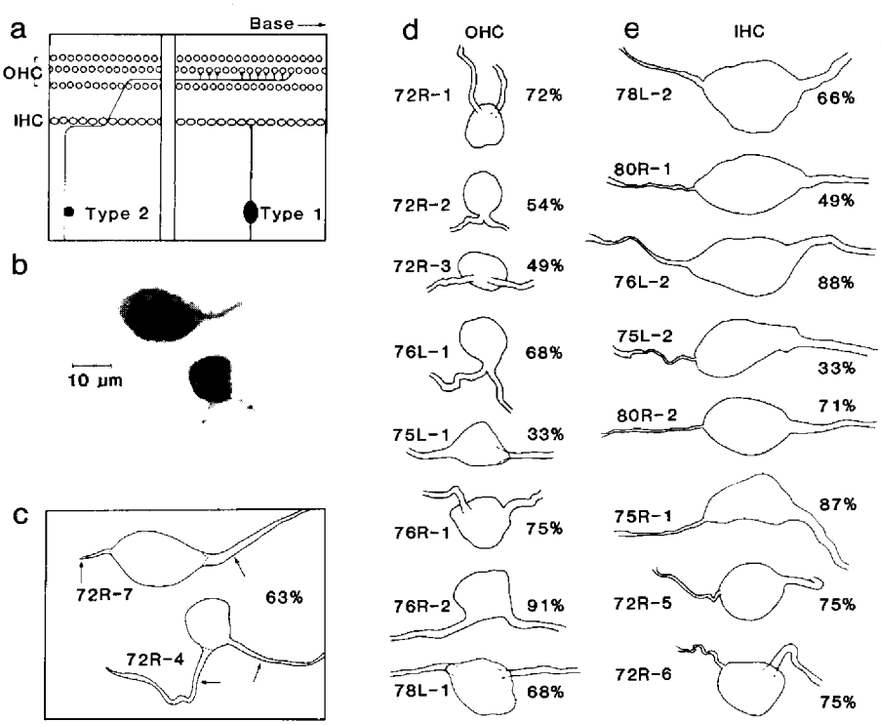

Fig. 1. Spiral ganglion cells in the cat cochlea. (a) Conceptualization of cochlear afferent innervation pattern. The type I (bipolar) neuron is shown projecting to IHC's and the type II (pseudomonopolar) neuron to OHC's. The diagram is not drawn to scale. (b) Photomicrograph of two neighboring labeled cells in the spiral ganglion of the middle turn. The peripheral processes are on the left and the central processes are on the right. The scale bar applies to (b) through (e). (c) Tracings of the photomicrograph in (b). The dotted lines show how cell body and processes are divided for the purpose of measuring cell area. The diameter of each process was measured at the narrowest points within 10 μm of the dotted lines. Cell area was determined by computerized planimetry. The arrows show where the diameters were measured for these two cells, which were located at a point 63 percent of the total distance from the base of the cochlea. (d) Camera lucida drawings of spiral ganglion cells with peripheral processes traced to OHC's. The drawings are arranged from top to bottom in order of increasing area of cell silhouette. Cell identification numbers are shown to the left and cell locations (percent distance from the base of the cochlea) are shown to the right. The dotted lines represent those portions of the processes partially obscured by the cell body but visible by focusing deeper into the section. (e) Camera lucida drawings of spiral ganglion cells with peripheral processes traced to IHC's. Drawings are labeled as in (d) and are arranged from top to bottom in order of decreasing area of cell silhouette.

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