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Improvement in Cognitive Functioning of Alcoholics Following Orthotopic Liver Transplantation

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Abstract

Cognitive functioning in alcoholic cirrhotics before and 1 year following orthotopic liver transplantation was compared with age- and sex-matched normal subjects. The alcoholic group improved significantly following transplantation on tests measuring psychomotor, visuopractic and abstracting abilities whereas the performance of normal controls remained virtually unchanged. In contrast, memory capacity in alcoholics with cirrhosis did not statistically improve following successful transplantation. Further investigation, using more sophisticated measures of memory function, are required to determine whether memory deficits are either associated with alcohol neurotoxicity or an irreversible component of hepatic encephalopathy. These findings suggest that a reversible hepatic encephalopathy underlies many of the neuropsychologic deficits observed in cirrhotic alcoholics and can be ameliorated following successful liver transplantation.

Keywords

Neuropsychologlc Deficits; Hepatic Encephalopathy; Alcoholic Cirrhosis; Liver Transplantation

Alcoholics commonly demonstrate a variety of neurocognitive disturbances.[1] Memory problems, abstracting deficits, visuopractic difficulties, and psychomotor inefficiency have been reported frequently in alcoholics using psychometric tests that are sensitive for detecting cerebral pathology.[2,3] Significantly, the magnitude of impairments does not correlate strongly with either the duration or intensity of alcohol abuse.[4] Furthermore, alcoholics who do not exhibit any of the medical complications frequently associated with longstanding excessive alcohol consumption typically perform normally on neuropsychologic tests.[5]

The absence of covariation between the duration of alcoholism and neurocognitive impairment, combined with the observation that medically healthy alcoholics are neurologically intact, as determined by neuropsychologic test performance, suggests that factors other than chronic excessive alcohol consumption may be responsible for the manifest disturbances. Recently, the presence of a chronic low grade hepatic encephalopathy has been implicated as a major contributory factor underlying the neuropsychologic deficits.[6] Moreover, the finding that biochemical measures of hepatic injury correlate with the severity of various neuropsychological deficits detected by formal neuropsychologic testing procedures,[7] and the observation that both cirrhotic alcoholics and nonalcoholics perform

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comparably on most neuropsychologic tests[8] suggests that advanced chronic liver disease is a major factor responsible for these neurologic deficits.

Liver transplantation affords a unique research paradigm in which the role of subclinical hepatic encephalopathy in the pathogenesis of the neuropsychologic impairments in alcoholics can be studied. If liver injury is the principal factor responsible for the impaired cognitive functioning, vis à vis an hepatic encephalopathy, it would be expected that a return to normal neuropsychologic test performance might ensue following replacement of the diseased liver with a functionally normal allograft. By quantifying the individual's neurocognitive competency both before and after hepatic transplantation, employing a battery of neuropsychologic tests, it should be possible to determine whether hepatic encephalopathy underlies the neurocognitive deficits observed commonly in alcoholic cirrhotics.

METHODS

Subjects

All subjects were recruited from among the population of patients returning to the University of Pittsburgh Health Sciences Center for their 1 year routine post-liver transplant follow-up examination. Thirteen subjects, 10 males and 3 females who had a pretransplant diagnosis of alcoholic (Laennec's) cirrhosis and who had completed a battery of neuropsychologic tests as part of their pretransplant neuropsychiatric evaluation, were recruited for study. Table 1 summarizes the age, education level, and IQ of this group of subjects. The diagnosis of alcoholic cirrhosis was confirmed in each by pathologic examination of the resected liver and a re-review of the initial history and physical findings. In addition, each subject was subjected to a comprehensive medical examination and a panel of biochemical tests assessing hepatic function and injury as well as other routine clinical laboratory parameters that are part of the routine transplant follow-up of such patients.

At the time of their pretransplant neuropsychologic testing, none of the patients were acutely encephalopathic according to the criteria of Parsons-Smith et al.[9] Also, each was free of any history of neurologic trauma or disease. In addition, no chronic medical illness, other than liver disease was present. Thus, apart from their advanced chronic liver disease, the alcoholic subjects were in good health prior to transplantation. The major criterion for liver transplantation was evidence of hepatic failure, as measured objectively by the following criteria: (1) expected survival of less than 1 year, (2) albumin <2.5 g/dl, (3) bilirubin >5.0 mg/dl, (4) ascites, and (5) recurrent varix bleeding. Following transplantation at the time of restudy, with the exception of one patient who had a recurrence of hepatitis B, none of the subjects reported the emergence of any new medical illness and none was experiencing a rejection episode.

The controls consisted of 13 age- and sex-matched individuals. They were recruited by advertisement. The control subjects were each tested twice with the two sessions being separated by about 1 year so as to equate the time interval between studies with the transplantation subjects. The test-retest interval for controls and the liver disease group is shown in Table 1. None of the control subjects had a history of chronic medical illness, neurologic injury or disease, or met criteria for alcohol abuse or dependence (see below).

All 26 subjects in this study participated on a voluntary basis and informed written consent was obtained. The study was approved by the University of Pittsburgh IRB in 1982.

Procedures

Psychiatric Assessment—At the time of the first evaluation, the NIMH Diagnostic Interview Schedule (DIS)[10] was administered to confirm a psychiatric diagnosis of alcohol abuse or dependence using DSM-III criteria in each of the alcoholic subjects and to rule out the presence of such disorder in the controls. Each of the alcoholic subjects had terminated his/her alcoholic beverage consumption at least 6 months prior to their participation in this study and consideration for transplantation; thus, the potential of alcohol withdrawal as a potential confounding factor on the test results was obviated. This extended period of sobriety prior to transplantation was a major criterion required for transplant candidacy and thus compliance was assured. The subjects were administered the DIS again at the time of their post-transplant evaluation approximately 1 year after successful transplantation. None of the subjects reported drinking alcoholic beverages at any time since the transplant surgery. Alcohol drinking history was obtained in each case by self-report in terms of quantity, frequency, and duration of consumption. This information was verified and found to be in accordance with information obtained from medical staff upon admission. The mean consumption level for the group was 6.44 (s = 4.24) absolute oz. of ethanol/daily for a mean duration of 17.4 (s = 10.0) years.

Although drinking behavior was assessed primarily through interview of the subject, corroboration of the validity of the information obtained was required, where possible, from informant interviews, as well as by a review of the medical record and from an assessment of indicators of recent drinking reflected in a panel of biochemical tests. Thus, while it is not possible to be completely certain about the absence of a drinking relapse, the data accrued from the various sources indicated that such did not occur in this sample.

Neuropsychologic Assessment—The amount of time elapsed between the first neuropsychologic testing and the liver transplantation surgery is shown in Table 1. Following an initial period of hospitalization, at which time, the patient's candidacy for transplantation was determined, the subjects were discharged to their homes or to a temporary residence and advised to be "on call." For possible immediate transplantation, the neuropsychologic evaluations were conducted during this initial hospitalization to determine transplant candidacy. Each subject was administered the same battery of 16 neuropsychologic tests on the two testing sessions. Neuropsychologic tests, like those included in this battery have been shown to be among the most sensitive methods available for detecting the presence of latent hepatic encephalopathy. A brief description of each of the tests and the rationale for their selection in this battery is included in Table 2 and has been described in detail elsewhere.[11, 12] The factors used in selecting the particular tests were their sensitivity, ease of administration, the presence of established norms, and the requirement for each test to be brief so that the results obtained would not be confounded either by subject fatigue or inattention and that each test was capable of being administered at the bedside. One limitation of the particular set of tests used in this study was that memory capacity was not extensively evaluated. In particular there was no measure of long-term delayed recall (eg, Rey-Osterreith Complex Figure Test) or an evaluation of short memory under conditions of distracting stimuli (eg, Brown Peterson Test). For each subject, the evaluation was conducted by a trained psychometrician usually in one session lasting approximately 2 hours.

Statistical Analysis

To document changes occurring between the two test sessions, a repeated measures multivariate analyses of variance (MANOVA) was employed. Where an overall significant *F* ratio was obtained, pairwise comparisons were conducted to determine the source of the effect.

In addition, to index magnitude of change, the percent difference from baseline score to the retest score was computed ($T_2 - T_1)/T_1 \times 100\%$). Next, aggregate scores were computed by averaging percent change scores on the psychomotor, visuopractic, perceptual speed and memory tests. The specific tests which were used to compose the four aggregate scores are listed in Table 2.

To conclude the analyses, the means and standard deviations of the normal control subjects were used to establish cutoff scores defining impaired performance. Impaired performance was defined as a score 1.5 SD or more below normal control performance. (This is equivalent to the lowest 10th percentile). The proportion of the alcoholic subjects performing in the impaired range was then computed at both the pre- and post-transplantation assessments.

RESULTS

The means and standard deviation for age, education and the Shipley WAIS equivalent IQ are summarized for each group in Table 1. The normal and alcoholic groups did not differ on any of these variables. Also, the test-retest interval was not different between the two groups.

The neuropsychologic test performance scores for the two groups along with the summary of the MANOVA are shown in Table 3. Significant Group × Time effects were found on 11 of the 16 neuropsychologic indices. In the normal group, performance decreased on one test, the time it took to read the list of words on the Stroop Test. Because the performance decrement on the Stroop test was a single isolated finding, it was concluded to have occurred as a result of chance. Otherwise, as can be clearly seen in Table 3, the mean scores were very similar across the two test sessions in the normals indicating that no practice effects existed. In contrast to these findings for the controls, significant improvement occurred between testing time points for individuals in the alcoholic group following transplantation. Improvement occurred on a total of 11 tests encompassing psychomotor, visuopractic, and perceptual speed processes. No change across test sessions was found, however, for memory capacity.

Analyses were next conducted to determine whether there were differences in level of improvement across specific categories of neurocognitive functioning. Fig. 1 presents the mean percent change from baseline for the aggregate scores in each of the four categories of tests included in the assessment battery. It is evident that improvement occurred for the alcoholics as compared with the normal controls on each dimension of neuropsychologic functioning with the exception of memory capacity. Overall, the performance scores of the normal subjects remained essentially unchanged whereas the alcoholics improved an average of 2l%.

The proportion of alcoholic subjects who were found to be impaired on tests of neuropsychologic functioning pre- and post-transplantation was determined also. Using the cut-off score of 1.5 SD below that of the controls, it can be seen in Fig. 2 that 40 to 60% of the subjects in the alcoholic group were impaired at the pretransplant assessment of the aggregate scores in one or more categories. Approximately 1 year following transplantation, between 10 and 20% of the alcoholic subjects were impaired on one or more categories of performance. Importantly, examination of the individual test performance revealed that two of the 13 alcoholics (15%) differed from the rest of the alcoholic group by remaining impaired on at least 50% of the tests following liver transplantation. Thus, apart from these two outliers, the improvement would have been greater than that reflected in Fig. 2.

DISCUSSION

This study demonstrates that neurocognitive capacity in cirrhotic alcoholic individuals substantially improves following successful orthotopic liver transplantation. An average increment of 21% across all tests to a level of normality after transplantation confirms the emerging evidence that indicates that some of the neuropsychologic deficits reported to occur commonly in alcoholics are primarily due to the presence of a low grade hepatic encephalopathy rather than alcohol induced brain injury.

Two important qualifications for this conclusion need to be emphasized. First, the reversibility observed was somewhat selective with regard to cognitive functioning. In this sample, memory capacity remained impaired at the post-transplantation assessment in the alcoholics suggesting that the mechanisms underlying these processes may involve factors other than those responsible for a subclinical hepatic encephalopathy. Alternatively, it is possible that the neuroanatomical substrate subserving memory capacities is permanently injured (either by alcohol or subclinical hepatic encephalopathy) whereas the type and severity of damage to the cerebrum subserving psychomotor, visuopractic and perceptual speed capacities affords the opportunity for recovery. Malnutrition and ethanol neurotoxicity are well recognized causes of neurologic pathology in alcoholics[13,14]; it may be that these two factors underlie the memory impairments herein reported. Further, it is possible, given that a sufficient interval of sobriety after transplantation has occurred, that even memory capacity may return to normal. Although this possibility cannot be discounted a priori, it is noteworthy that alcoholics have been found to have deficient memory capacities even after 5 years of continuous sobriety.[15] These results should be interpreted cautiously because of the lack of extensive memory testing. The memory tests employed in this study do not comprehensively capture all aspects of memory function. Future studies are necessary to determine whether memory deficits are truly nonreversible.

Second, it is interesting to note that not all alcoholic individuals demonstrated cognitive recovery post-transplantation. Two of 13 individuals in this sample accounted for a significant proportion of the residual deficits observed postsurgically. The reasons for the observed impairment following transplant in these two individuals could not be determined; however, it is well recognized that the alcoholic population is heterogeneous. Importantly, drinking history of these two individuals was comparable to the rest of the group. Individual differences in the population with respect to susceptibility to alcoholic cirrhosis[16] as well as the neuropsychologic sequelae of alcoholism[17] are known to exist but poorly understood. To the extent that neuropsychologic test performance is somewhat predictive of social and vocational adjustment,[18] it is important for future research to be able to identify alcoholic individuals who will not recover cognitively following liver transplantation. In this study, it was not possible to determine whether the subjects who recovered neurocognitively were different post-transplantation with respect to psychosocial adjustment from those who did not recover because of the small sample size. Nonetheless, this avenue of research may have important ramifications in its ability to identify candidates most suitable for transplantation as defined by their potential for cognitive rehabilitation.

Four additional issues need to be considered in interpreting the findings. One important concern pertains to the content of the neuropsychologic test battery. Both practical time constraints as well as stamina limitations due to the patient's medical condition necessarily prevented an in-depth quantitation of all neurocognitive processes. For example, language skills and abstracting abilities were not specifically evaluated in this study. It is plausible that these or other capacities do not recover following successful transplantation. Thus, it is essential that the findings reported herein are not over-generalized to assume recovery

across all cognitive processes. It may be that other cognitive processes not measured in this battery do not recover following transplantation.

Secondly, the improvement observed in neurocognitive function could be confounded by the improved affective state of the individual following transplant. In the pre-transplant state, one is faced with the presence of a life-threatening illness and may experience severe anxiety or depression which could in turn affect neurocognitive status. In each case, the DIS was used to determine the presence of any diagnosable psychiatric disorders. No current symptomatology of psychiatric disorders was reported for any subject. Where there was a history of psychiatric disorder, the age of onset of the disorder preceded the age of onset of liver disease. The stress of hospitalization could also adversely affect neuropsychologic test performance.

Another potential factor which potentially could have accounted for the neurocognitive improvements observed is simply the elapsed time and not the re-establishment of normal liver function. While this possibility cannot be discounted entirely, it is not a highly likely explanation for the results. As noted previously, the alcoholics were abstinent from alcohol for at least 6 months prior to their initial testing; this is the period of time within which the most substantial spontaneous recovery of neuropsychologic deficits occurs in alcoholics with sobriety.[19] Following this interval, comparatively little additional improvement typically takes place in abstinent alcoholics.[20] Hence, it is reasonable to conclude that by the time of the initial assessment, the alcoholics were in a chronic state of persisting neurocognitive impairment, and had already achieved their optimal amount of cognitive recovery concomitant with alcohol abstinence. Whether a follow-up assessment at a later interval (perhaps 2–3 years) would reveal even more significant cognitive recovery will be a matter of future investigations. An additional test of our hypothesis would be to measure the performance of a nonoperated control group of alcoholics who also demonstrated cognitive impairment. Although theoretically attractive, such a test would not be logistically (or ethically) possible given the severity of the medical condition of cirrhotic alcoholics awaiting transplant in our facility.

Another complicating factor is the cyclosporine treatment used following transplantation. Tremor and impaired fine motor control have been reported to occur in post-transplant patients who are on cyclosporine. Because the patients in this study were all on a standard dose of cyclosporine (7–9 mg/kg/day), it is probable that this psychomotor performance might have been even better than it was without this mitigating factor. In any event, the motor capacities, measured by the tests in this investigation, were not impaired in the alcoholics studied post-transplantation. It should be noted that persisting static ataxia has been reported in a previous study of nonalcoholics who have survived hepatic transplantation.[21] Two recent reports have documented improvement in hepatic encephalopathy following orthotopic liver transplantation in nonalcoholic cirrhosis[21] and hepatocerebral degeneration.[22]

The demonstration that cognitive recovery can occur in alcoholics has important practical implications. First, the specific aspects of the liver disease underlying the neurocognitive deficits are in need of clarification. For example, while it has been generally assumed, for example, that latent portal-systemic encephalopathy consequential to portal venous shunting of blood in cirrhotics is the primary etiological mechanism, it is noteworthy that an association between vitamin E deficiency and impaired psychomotor functioning in patients with cholestatic liver disease has been reported.[23] Thus, extrahepatic as well as intrahepatic factors may underlie in some complex fashion the apparent “hepatic” encephalopathy of patients with advanced liver disease. The extent to which correction of an occult vitamin E deficiency as well as other nutritional deficiencies vicariously occurs as a result of liver

transplantation and was contributed to the improvement observed in neuropsychologic test performances revealed in this study is unknown. Second, it suggests the need for intensive medical management of alcoholic liver disease as part of an overall rehabilitation program for the vast majority of alcoholic individuals who, for whatever reason, do not qualify for liver transplantation. This currently is not standard practice in psychiatric or rehabilitation facilities. In light of the importance of intact neurocognitive functioning for optimal everyday functioning, it would appear essential to integrate and coordinate medical and psychosocial treatments. Third, the results obtained in this investigation provide further justification for liver transplantation of alcoholic individuals. It has been recently reported that alcoholic patients can be transplanted successfully and that a substantial proportion of survivors are employed and in good health.[24] Although the findings reported herein must be considered preliminary and should be replicated, the cognitive improvement observed in alcoholics following transplantation may be an important mediating factor for psychosocial adjustment following transplantation.

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References

1. Tarter, RE.; Arria, AM.; Van Thiel, DH. Neurobehavioral disorders associated with chronic alcohol abuse. In: Goedde, Agarwal DP., editor. Alcoholism: Biomedical and Genetic Aspects. Elmsford, NY: Pergamon Press; 1990. p. 113-129.
2. Wilkinson, D.; Pavlos, C. The chronic effects of alcohol on memory: A contrast between a unitary and dual system approach. In: Galanter, M., editor. Recent Developments in Alcoholism. New York: Plenum Press; 1987. p. 5-26.
3. Parsons, O.; Farr, S. The neuropsychology of alcohol and drug use. In: Filskov, S.; Boll, T., editors. Handbook of Clinical Neuropsychology. New York: Wiley; 1981. p. 320-365.
4. Bergman, H. Brain dysfunction related to alcoholism: Some results from the KARTAD project. In: Parsons, O.; Butters, N.; Nathan, P., editors. Neuropsychology of Alcoholism: Implications for Diagnosis and Treatment. New York: Guilford Press; 1987. p. 21-44.
5. Grant I, Adams K, Reed R. Normal neuropsychological abilities of alcoholic men in their late thirties. Am J Psychiatry 1979;136:1263–1269. [PubMed: 484720]
6. Tarter RE, Van Thiel DH, Arria AM, Carra J, Moss H. Impact of cirrhosis on the neuropsychological test performance of alcoholics. Alcohol Clin Exp Res 1988;12:619–621. [PubMed: 3067603]
7. Tarter RE, Hegedus A, Van Thiel DH, Gavaler J, Schade R. Association between hepatic dysfunction and neuropsychological test performance in alcoholics with cirrhosis. J Stud Alcohol 1986;47:74–77. [PubMed: 3959562]
8. Rehnstrom S, Simert G, Hansson J, Johnson G, Vang J. Chronic hepatic encephalopathy: A psychometrical study. Scand J Gastroenterol 1977;12:305–311. [PubMed: 866992]
9. Parsons-Smith B, Summerskill W, Dawson A, Sherlock S. The electro-encephalograph in liver disease. Lancet 1957;1:867–871. [PubMed: 13482229]
10. Robins LN, Helzer JE, Croughan J, Ratcliff KS. National Institute of Mental Health Diagnostic Interview Schedule. Arch Gen Psychiatry 1981;38:381–389. [PubMed: 6260053]
11. Tarter RE, Hegedus A, Van Thiel D, Schade R, Gavaler J. Nonalcoholic cirrhosis associated with neuropsychological dysfunction in the absence of overt evidence of hepatic encephalopathy. Gastroenterology 1984;86:1421–1427. [PubMed: 6714571]
12. Lezak, M. Neuropsychologic Assessment. 2. New York: Oxford University Press; 1982.
13. Anatow, D.; McClain, C. Nutrition and alcoholism. In: Tarter, R.; Van Thiel, DH.; Edwards, K., editors. Alcohol and Brain: Chronic Effects. New York: Plenum Press; 1985. p. 81-120.

14. Walker D, Hunter B, Abraham W. Neuroanatomical and functional deficits subsequent to chronic ethanol administration in animals. Alcohol Clin Exp Res 1981;5:267–282. [PubMed: 7018310]
15. Muuronen A, Bergman H, Hindmarsh T, Telakivi T. Influence and improved drinking habits on brain atrophy and cognitive performance in alcoholic patients: A 5-year follow-up study. Alcohol Clin Exp Res 1989;13:137–141. [PubMed: 2646967]
16. Saunders JB, Williams R. The genetics of alcoholism: Is there an inherited susceptibility to alcohol related problems. Alcohol Alcohol 1983;18:189–217.
17. Blass JP, Gibson GE. Abnormality of a thiamine requiring enzyme in patients with Wernicke-Korsakoff Syndrome. N Engl J Med 1977;279:1367–1370. [PubMed: 927453]
18. McCrady BS, Smith DE. Implications of cognitive impairment for the treatment of alcoholism. Alcohol Clin Exp Res 1986;10:145–149. [PubMed: 3521371]
19. Allen RP, Faillace LA, Reynolds DM. Recovery of memory functioning in alcoholics following prolonged alcohol intoxication. J Nerv Ment Dis 1971;153:417–423. [PubMed: 5123712]
20. Brandt J, Butters N, Ryan C, Bayog R. Cognitive loss and recovery in chronic alcohol abusers. Arch Gen Psychiatry 1983;40:435–442. [PubMed: 6838323]
21. Tarter RE, Switala J, Arria AM, Plail J, Van Thiel DH. Subclinical hepatic encephalopathy: Comparison before and after orthotopic liver transplantation. Transplantation 1990;50:632–637. [PubMed: 2219286]
22. Powell EE, Pender MP, Chalk JB, Parkin PJ, Strong R, Lynch S, Kerlin P, Cooksley G, Cheng W, Powell LW. Improvement in chronic hepatocerebral degeneration following liver transplantation. Gastroenterology 1990;98:1079–1082. [PubMed: 2311862]
23. Arria AM, Tarter RE, Warty VS, Van Thiel DH. Vitamin E deficiency and psychomotor dysfunction in adults with primary biliary cirrhosis. Am J Clin Nutr 1990;52:383–390. [PubMed: 1973868]
24. Kumar S, Stauber RE, Gavaler JS, Basista MH, Dindzans VJ, Schade RR, Rabinovitz M, Tarter RE, Gordon R, Starzl TE, Van Thiel DH. Orthotopic liver transplantation for alcoholic liver disease. Hepatology 1989;11(2):159–164. [PubMed: 2307394]

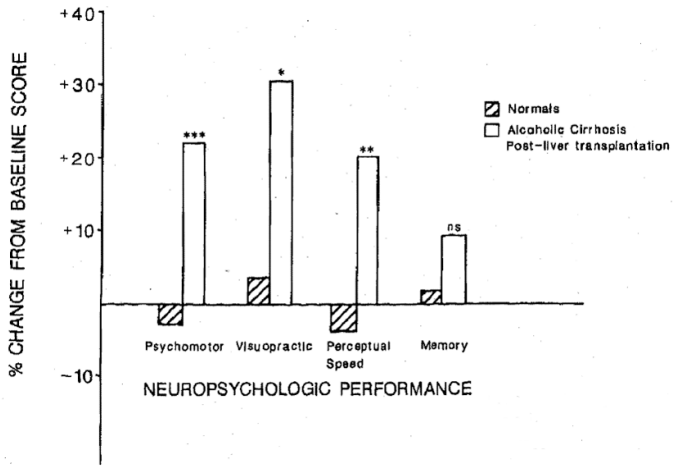

Fig. 1.

Percent change from baseline score on neuropsychologic tests across dimensions of function. Within each dimension, scores were averaged for form four aggregate scores (see Table 2 for components of aggregate scores).

ns: not significantly different

* $p<.05$

** $p<.01$

*** $p<.005$

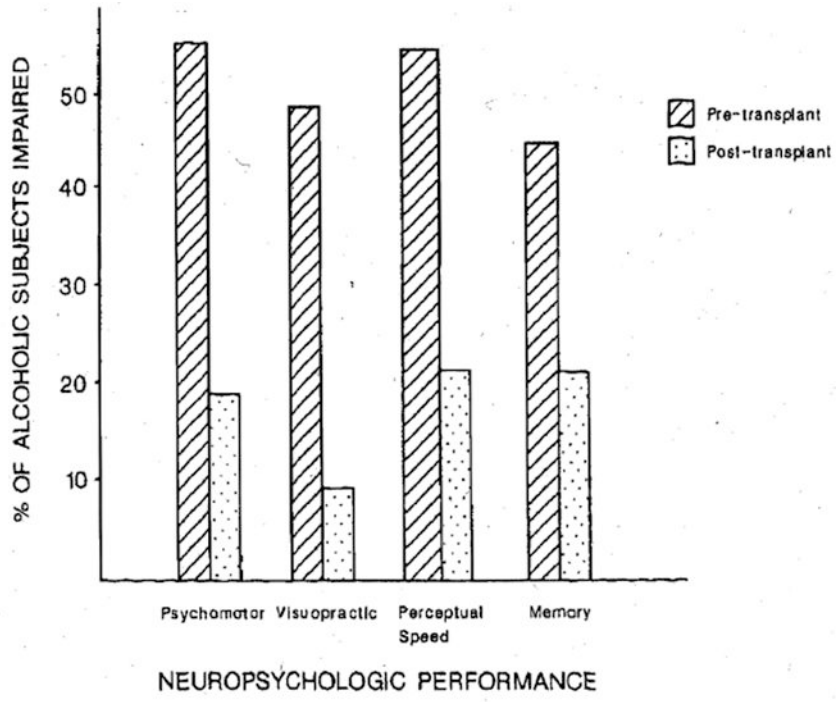

Fig. 2.

Percent of alcoholic subjects who were clinically impaired (1.5 SD below normal) pre- and post-transplantation. (As in Figure 1, scores were averaged across four dimensions.)

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Table 1

Characteristics of the Alcoholics and Normal Controls

	Alcoholics (*N* = 13)		Normals (*N* = 13)			
	X	**(s)**	**X**	**(s)**	***F***	***p***
Age (years)	39.69	(6.70)	43.85	(9.01)	1.78	NS*
Education level (years)	12.54	(0.97)	13.15	(1.72)	1.26	NS
Shipley Scale IQ (WAIS equivalent)	107.67	(6.12)	112.04	(5.73)	2.93	NS
Test-retest interval (months)	13.77	(6.76)	12.92	(3.17)	1.88	NS
Interval between neuropsychologic testing and surgery (weeks)	2.71	(4.94)				

*NS, not significant.

Table 2

Description of Neuropsychologic Tests

Psychomotor function	
Signature time	The score obtained on this test is simply the amount of time required to sign one's name. Both dominant and nondominant signature time is measured.
Finger tapping	This test of simple motor speed consists of a telegraph key attached to a counter. The subject is instructed to tap the key as quickly as possible. Five trials, each of 10 sec duration, are given for each hand. The score is the mean number of key depressions or taps across five trials for both hands.
Grooved pegboard	This test measures eye-hand coordination. The subject is required to insert pegs into a form board having notched holes. The pegs can thus only be placed in the form board in a certain way. The time required to place all of the pegs in the pegboard for the dominant hand is recorded.
Visuopractic capacity	
Block design	This test requires the subject to arrange a set of nine identical cubes (red on two sides, white on two sides and half red, half white on two sides) according to the pattern on each of 10 sample cards of increasing difficulty with extra credit for speed and a time limit for each design.
Trailmaking A	This test requires the subject to traverse a complex spatial field by serially connecting numbers. The time required to complete the task is recorded.
Trailmaking B	This test is given subsequent to Trailmaking A and requires the subject to alternate numbers and letters in a manner similar to that used in Trailmaking A. The letters and numbers are arranged haphazardly on a sheet of paper. The time required to complete the task is recorded.
Perceptual speed	
Stroop interference	This test consists of three separate parts. First, the subject is required to read a series of words (blue, green, red) printed on a card. The second part consists of reading color patches (xxx), and the third is an interference task where the subject reads the color of the ink of the printed word. The time required to successfully complete the task is measured, along with the number of errors made.
Symbol digit	This test requires sustained attention and visual-scanning abilities. The subject must write in sequence, as rapidly as possible, numbers that correspond to a particular symbol. The person must continuously scan the symbol number matchings at the top of a page, while placing in a row of boxes below the correct number where only the symbol is present. The number of correct responses obtained in 90 sec is recorded.
Memory	
Digit span	This test is a measure of immediate memory capacity. The subject is asked to repeat in a forward order and then in backward order a string of numbers of increasing length verbally presented by the examiner. The score for either direction is the longest sequence that the person can recall.
Benton visual retention test	Of this test of short-term visual memory for figural information, the subject is given 10 sec in which to study a geometric figure, after which the stimulus is removed and he/she must draw the figure from memory on a sheet of paper. Standardized instructions for scoring this test are described in the test manual.

Table 3

Means and SDs of Neuropsychologic Test Results for Each Group and Results of Repeated Measure MANOVA

	Normal controls				Alcoholics				MANOVA Results		
	1st Assessment		Re-Test		1st Assessment		Re-test				
	$\bar{X}$	(s)	$\bar{X}$	(s)	$\bar{X}$	(s)	$\bar{X}$	(s)	Group effect *F*	Time effect *F*	Group × Time *F*
Psychomotor function											
Signature time (sec) (dominant hand)	6.08	(1.71)	6.38	(1.89)	7.42	(2.69)	7.92	(4.56)	1.05	0.23	0.02
Signature time (sec) (nondominant hand)	14.69	(6.07)	16.54	(6.96)	24.58	(11.65)	16.17	(9.41)	1.60	5.04*	9.85‡
Finger tapping (response) (dominant hand)	48.67	(7.39)	46.00	(7.58)	43.38	(14.85)	49.27	(9.86)	0.23	2.94	6.56†
Finger tapping (responses) (nondominant hand)	42.08	(6.16)	42.08	(9.17)	37.25	(10.62)	46.60	(6.38)	0.00	7.97†	7.97†
Grooved pegboard (sec) (dominant hand)	67.91	(10.14)	67.31	(9.76)	109.67	(47.60)	76.75	(13.80)	9.48*	7.50†	5.20*
Grooved pegboard (sec) (nondominant hand)	69.17	(9.39)	66.15	(8.00)	130.70	(80.10)	83.73	(17.22)	9.11*	5.15*	4.26*
Visuopractic capacity											
Block design (derived score)	36.67	(7.04)	37.31	(6.58)	27.31	(7.31)	34.85	(5.05)	7.22†	10.15‡	5.95*
Trailmaking A (sec)	28.38	(11.00)	23.46	(7.75)	52.85	(28.71)	34.38	(16.04)	9.26‡	9.26‡	3.10
Trailmaking B (sec)	67.00	(23.06)	61.23	(23.59)	121.15	(65.64)	77.69	(23.83)	7.79†	8.73†	5.12*
Perceptual speed											
Stroop words (sec)	9.42	(1.78)	10.42	(1.93)	12.85	(4.65)	11.58	(2.68)	4.86*	0.32	6.25*
Stroop colors (sec)	13.67	(2.42)	13.50	(2.15)	20.38	(8.80)	14.25	(2.26)	6.38*	7.14†	6.45*
Stroop Interference (sec)	25.42	(7.50)	24.25	(6.45)	35.08	(12.69)	23.33	(4.31)	2.75	16.52‡	11.4‡
Symbol digit (no. correct)	50.33	(8.96)	52.38	(12.81)	31.83	(12.69)	45.17	(9.46)	9.66‡	14.03‡	7.66†
Memory											
Digit span forward	7.08	(1.04)	7.38	(1.12)	6.15	(1.52)	6.08	(0.99)	7.49†	0.44	0.44
Digit span backward	5.00	(1.15)	4.76	(1.42)	4.15	(1.14)	4.00	(1.13)	4.59*	0.20	0.93
Benton visual retention test (no. correct)	7.75	(1.60)	7.83	(1.34)	5.55	(1.86)	6.45	(1.81)	8.11†	2.98	2.06

*$p < 0.05$.

†$p < 0.01$.

‡$p < 0.005$.