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# Assessment of Olfactory Deficits in Detoxified Alcoholics

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DITRAGLIA, G. M., D. S. PRESS, N. BUTTERS, T. L. JERNIGAN, L. S. CERMAK, R. A. VELIN, P. K. SHEAR, M. IRWIN AND M. SCHUCKIT. *Assessment of olfactory deficits in detoxified alcoholics.* ALCOHOL 8(2) 109–115, 1991.—Olfactory functioning was evaluated in 37 male detoxified alcoholics and in 21 age-matched nonalcoholic controls using the University of Pennsylvania Smell Identification Test (UPSIT). Of the original subjects, 23 alcoholics and 14 controls returned for reevaluation 3–4 months following initial testing. The results showed that alcoholics had significantly lower UPSIT scores than did the controls, both at baseline and follow-up testing. Thirty-two percent of the alcoholics' UPSIT scores, in comparison to five percent of the controls' scores, fell into the clinically impaired range. Although current smoking patterns correlated significantly with UPSIT indices, comparisons limited to nonsmokers still indicated that the alcoholics were significantly impaired on this olfactory task. Correlational analyses indicated that olfactory performance was unrelated to alcoholics' scores on visuoconceptual and language tasks. Correlations with MR-derived indices of CSF volume showed a highly significant relationship between UPSIT scores and cortical sulcal volumes. Additionally, alcoholics (N = 15) who remained abstinent had significantly higher scores at follow-up than those who were not abstinent (N = 8). These findings demonstrate that alcoholism is associated with basic olfactory impairments which are only partially reversible with abstinence and that cortical structures play an important role in this sensory loss.

Ethanol Olfaction Abstinence UPSIT Magnetic Resonance Imaging

ALTHOUGH disorders of olfaction have been the least formally studied and the most clinically neglected of all sensory deficits (33), recent studies involving a standardized test of odor identification demonstrate that deficits in olfaction exist in many disease states. Patients with Alzheimer's disease (6,40), Parkinson's disease (5), multiple sclerosis (7), Down's syndrome (39), and schizophrenia (15,24) have all been reported to have severe olfactory impairments, and these deficits may be important early signs of the pathological conditions underlying some of these disorders. Among alcoholic populations there is abundant evidence that individuals with Korsakoff's syndrome are impaired on a variety of odor identification (7, 21, 25), odor quality discrimination (21,29), odor intensity scaling (20,22) and olfactory recognition and recall tests (13). In many cases, the Korsakoff patients' olfactory deficits have been attributed to damage to the medial diencephalic nuclei which form an important part of the neuroanatomical circuit mediating this sensory modality (20–22).

Despite this interest in the olfactory deficiencies associated with Korsakoff's syndrome, there has been little systematic assessment of olfactory functions in nonamnesic alcoholics. Moreover, those studies that have been attempted have not yielded totally consistent results. Investigations focusing upon Korsakoff's syndrome have reported comparable performances between nonamnesic alcoholic and normal control subjects on a variety of olfactory measures (13, 20–22), whereas Potter and Butters (29) reported that alcoholics performed significantly worse than normal controls on tests of butanol threshold detection. These mixed findings may stem from differences in methodology, failure to control for the effects of smoking, and small sample sizes (26). Doty and his colleagues (7) also suggest that since the olfactory tests employed in each study were not standardized, unreliable results and only semiquantitative data may have been reported.

The aim of the present study is to evaluate olfaction in a large sample of alcoholics participating in an inpatient VA Alcohol Treatment Program and to attempt to determine whether at least 3 months of abstinence has any effect on these alcoholics' olfactory ability. A carefully screened group of alcoholics were administered The University of Pennsylvania Smell Identification Test (UPSIT) during treatment and again several months later

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(7,8). The UPSIT is a standardized test of olfaction which correlates significantly with traditional odor detection thresholds (7) and has high test/retest reliability (r = .90).

Since the UPSIT may involve cognitive as well as sensory abilities, its association with neuropsychological tests known to be sensitive to alcohol abuse was assessed. Significant correlations between impairments on the UPSIT and these cognitive measures would suggest that the alcoholics' performance on this identification task might be reflecting changes in cognitive, rather than sensory, functions. In contrast, a failure to find any associations between olfactory and cognitive scores would suggest that any olfactory deficiencies noted may represent a true sensory loss. Also, since olfactory deficits in man have been associated with both subcortical and cortical dysfunction (5, 6, 20–23), the relationship between performance on the UPSIT and indices of cortical sulcal and ventricular CSF volumes derived from Magnetic Resonance Imaging (MRI) were assessed.

## METHOD

### *Subjects*

Thirty-seven alcoholic males were used in this study. These patients had undergone detoxification (Mean = 9.9 days since last drink, SD = 7.4) prior to admission to the San Diego Department of Veterans Affairs Medical Center's Inpatient Alcohol Treatment Program (ATP), a 28-day program for alcoholism counseling and treatment. Librium was administered to many of the patients during detoxification, but all patients had ceased using this medication for at least 48 hours prior to their participation in this investigation.

Using the Alcohol Research Center Intake Interview (34), medical and drinking history data were obtained from each patient and at least one resource person such as a close friend or family member, and the diagnosis of alcohol abuse or dependence was documented using DSM-III criteria. In the few cases (less than 10%) when there were disagreements in the histories provided by the patient and the resource person, the more severe of the two reports was recorded (e.g., the more recent date of last drink or the heavier alcohol consumption). Individuals were excluded from this study if they had a history of overt liver (e.g., cirrhosis, jaundice), metabolic (e.g., diabetes), vascular (e.g., coronary artery disease), or neurologic (e.g., head injury, encephalitis, epilepsy) disorders. Patients with a history of drug abuse or of major psychiatric illness (e.g., schizophrenia, bipolar affective disorder) predating the onset of alcoholism were also screened from the study. A brief neuropsychological examination comprised of four tests (WAIS-R Vocabulary, Trails A and B, WAIS Digit Symbol) often affected in recently detoxified alcoholics (32) was administered to each alcoholic within 48 hours of admission.

Twenty-one nonalcoholic male controls were recruited from the community by newspaper advertisements. All of these control subjects were screened with the Alcohol Research Center Intake Interview (34) for a history of alcohol abuse, alcoholism, drug abuse and the same medical and psychiatric disorders described for the alcoholic subjects. The controls were administered the same neuropsychological examinations as the alcoholics and received monetary compensation for their participation.

Table 1 shows the mean age, education, drinking histories, and neuropsychological test scores for the 37 alcoholics and 21 controls. Since the two groups' difference in education approached significance ($p<0.06$), analyses of covariance controlling for education were used to compare their performances on the neuropsychological tests. As expected, the alcoholics were impaired on most of the test scores, and thus, appeared similar on the basis of their cognitive deficits, as well as their drinking history, to patients reported in other neuropsychological studies involving alcoholics (32).

TABLE 1

MEAN AGE, EDUCATION, DRINKING VARIABLES, AND NEUROPSYCHOLOGICAL TEST SCORES FOR ALCOHOLICS (N = 37) AND NONALCOHOLIC CONTROLS (N = 21)

| | Alcoholics | Controls | $p$* |
|---|---|---|---|
| Age (Years) | 49.9 (9.6) | 50.6 (10.5) | NS |
| Education (Years) | 14.0 (1.8) | 14.9 (1.6) | <0.06 |
| Years of Alcoholism | 13.7 (9.8) | — | — |
| Daily Ethanol Consumption (average number drinks per day) in 3 months prior to admission | 14.2 (9.9) | 0.4 (0.7)† | <0.00 |
| Vocabulary (WAIS-R Scaled Score) | 9.9 (2.3) | 11.7 (1.9) | <0.03‡ |
| Trails A (Seconds) | 31.0 (9.7) | 26.0 (7.0) | <0.06 |
| Trails B (Seconds) | 105.8 (45.8) | 74.1 (28.8) | <0.01 |
| Digit Symbol (WAIS Scaled Score) | 8.9 (2.0) | 11.3 (2.6) | <0.00 |

*Age, Education and Daily Ethanol Consumption were assessed with two-tailed $t$-tests; Neuropsychological Test scores with analysis of covariance controlling for educational differences.

†Daily ethanol consumption for the 3 months prior to the interview was available for only 20 of the 21 nonalcoholic controls.

‡Indicates significant covariate (education) effect.

### *Procedure*

All alcoholics were administered the UPSIT initially during their third or fourth week in the treatment program (i.e., baseline evaluation); those alcoholics who returned for their follow-up evaluations (Mean = 102.5 days after discharge; SD = 13.6) received the UPSIT a second time. All nonalcoholic controls received the UPSIT and the other cognitive tasks during a single initial test session; those controls who returned for their follow-up assessments (Mean = 131.5 days after initial testing; SD = 25.2) were evaluated with the UPSIT for a second time. All of the subjects had MR evaluations of their brains at the time of their baseline UPSIT assessments. However, nine of the alcoholics' and six of the controls' MR images could not be used because of excessive movement during imaging, equipment failures or other technical problems. Both groups received monetary compensation for their follow-up testing.

The UPSIT is a standardized microencapsulated odor test consisting of four booklets containing 10 odorants apiece, one odorant per page (7, 8, 35). A multiple-choice question with four response alternatives for each item is located above each "scratch and sniff" odorized strip. For each of the 40 items, the subjects sniffed the odorant and then indicated which one of the four alternatives the odor represented. The UPSIT was individually self-administered by each subject in the presence of an examiner, who prefaced administration with general verbal instructions and a demonstration. If an item was skipped, the subject was instructed to complete the missing item. All subjects completed the test within 20 minutes. Since current smoking has been reported to be significantly related to UPSIT scores (7), an attempt was made to collect relevant smoking information (average number of cigarettes currently being smoked per day) on each subject.

Magnetic Resonance Imaging (MRI) was performed with a 1.5-T super-conducting magnet (Signa; General Electric, Milwaukee), at the UCSD/AMI Magnetic Resonance Institute. A standard protocol was used for the acquisition of MR brain images, and the images were analyzed in the Brain Image Analysis Laboratory of the Department of Psychiatry, UCSD. Proton-density weighted (PDW) and T2-weighted (T2W) images were obtained simultaneously for each section, using an asymmetrical, multiple-echo sequence (TR = 2000 ms, TE = 25, 70 ms) to obtain images of the entire brain in the axial plane. Section thickness was 5 mm with a 2.5 mm gap between sections in all instances. A 256 × 256 matrix and 24 cm field of view were used. The MRI cranial volumes were calculated using all slices in the full axial sequence. No sedation was administered for the examinations.

A detailed description of the basic image analysis method has been reported previously (17). Only a brief summary is provided here: Each axial image is first digitally filtered to reduce the signal drift across the image due to magnetic field and gradient inhomogeneities. Information in the two images for each axial section is then combined to best distinguish the different tissues in the image. Since CSF has very low signal values in the PDW image and very high values in the T2W image, a subtraction of the images provides good separation of CSF from other tissues. For each section imaged, a computed matrix is produced. In this matrix, pixels are classified as most resembling (in signal strength) grey matter, white matter, CSF, or signal hyperintensities (tissue abnormalities). The full series of axial images is analyzed, beginning at the bottom of the cerebellar hemispheres and extending through the vertex.

Further manipulations to derive the specific structural measures for the present study are then made using these "pixel-classified" images. Trained operators, blind to any subject characteristics, use a stylus-controlled cursor on the displayed images to manually separate infratentorial (cerebellar) from supratentorial areas, left from right hemispheres, and the cortical from subcortical regions of the supratentorial cranium. For the present study, all pixels designated as CSF in the subcortical regions of all sections were summed for an estimate of ventricular volume. Similarly, all CSF pixels in the cortical zone were summed to estimate cortical sulcal volume. Each of these was expressed as a proportion of the supratentorial cranial volume.

These measures were converted to age-corrected Z-scores using formulae derived from data in 58 normal volunteers (17). This involved using polynomial regression analyses to estimate means and standard deviations of the CSF proportions across the age range. Using these results, each subject's ventricular (and cortical) CSF proportion was expressed as a deviation from the normal mean expected for the subject's age, and the deviation was divided by the standard deviation expected at this age. These values, by definition, have an expected mean of 0 and a standard deviation of 1 in the controls. The group means presented here are the averages of these Z-scores. The computation of such age-adjusted scores is described in greater detail in earlier reports (19,28). Correlations were computed between these Z-scores and UPSIT scores.

## RESULTS

### *Olfactory Function During Treatment (Baseline)*

The distributions of baseline UPSIT scores for alcoholic and control subjects are presented in Fig. 1. A two-tailed *t*-test revealed that alcoholics were significantly impaired on this measure, relative to controls ($p<0.007$). The group means were 34.1 (SD = 5.2) and 37.5 (SD = 2.2) in the alcoholics and controls, respectively.

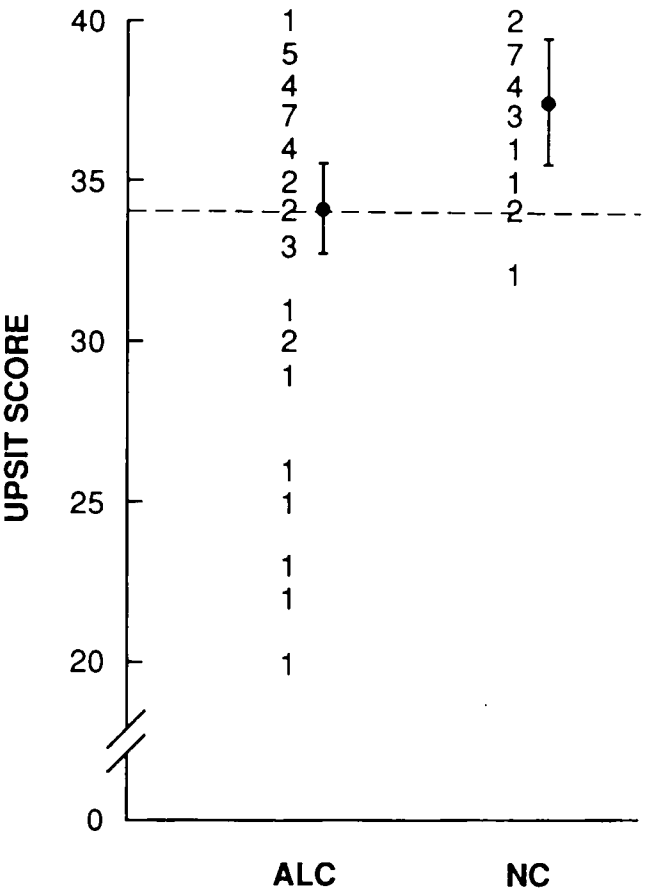


FIG. 1. Frequency distributions of UPSIT scores for alcoholics (N = 37) and nonalcoholic controls (N = 21). The horizontal line drawn at 34 correct separates those subjects with normal scores from those with clinically significant olfactory deficits. Numerals refer to the number of individuals within each group obtaining a given score. Vertical bars to the right of the numbers indicate the 95% confidence levels. The black dots note the mean UPSIT score for each group.

In order to investigate the clinical significance of this strong group effect, each subject was classified as either demonstrating normal or impaired olfaction. As suggested by normative data presented in the UPSIT manual (35), scores falling between 34 and 40 were classified as normal and those falling below 34 were classified as representing clinically significant impairment. Figure 1 illustrates that 12 of the 37 alcoholics (32.4%) achieved scores that fell into the impaired range, while only 1 of the 21 controls (4.8%) received this classification. A chi-square test revealed that this increased prevalence of clinical impairment in the alcoholic group, compared to the control group, was highly significant ($p = 0.01$).

To determine if the olfactory deficit observed in the alcoholics was related to their cognitive functioning, the UPSIT baseline scores of the alcoholics were correlated with their neuropsychological test scores. As shown in Table 2, UPSIT baseline score did not correlate with any neuropsychological test score, although there were significant intercorrelations between individual neuropsychological tests. A similar correlational analysis was not attempted for the nonalcoholic controls because of the relatively small number of subjects (N = 21) and their near-perfect UPSIT scores (i.e., 9 of the 21 controls earned scores of 39 or 40).

Since current smoking habits affect performance on olfac-

TABLE 2

CORRELATION MATRIX OF ALCOHOLICS' (N = 37) BASELINE UPSIT SCORE WITH SCORES ON THE NEUROPSYCHOLOGICAL TESTS ADMINISTERED WITHIN 48 HOURS OF ADMISSION

| | UPSIT | Trails A | Trails B | Digit Symbol |
|---|---|---|---|---|
| UPSIT | — | | | |
| Trails A | −.25 | — | | |
| Trails B | −.19 | .44* | — | |
| Digit Symbol | .14 | −.54* | −.47* | — |
| Vocabulary | .26 | .13 | −.30 | .08 |

*Denotes $p<0.01$.

tory tests (7), the possible contribution of smoking to the group differences on the UPSIT was assessed. Smoking data were not available for two of the alcoholic subjects and one of the normal controls; these subjects were, therefore, excluded from the following analyses. In the remaining sample, 69% (N = 24) of the alcoholic subjects and 20% (N = 4) of the controls reported current smoking, a difference which reaches statistical significance when analyzed with a chi-square test ($p<0.001$). In addition, those alcoholics who did smoke reported that they consumed a significantly greater number of cigarettes per day than did the controls who smoked ($p<0.001$). The group means for daily cigarette consumption were 15.5 (SD = 2.2) and 2.2 (SD = 3.0) for the alcoholic and nonalcoholic control subjects, respectively. Pearson product-moment correlation coefficients suggest that UPSIT scores and daily cigarette consumption are significantly related ($r = -.41$, $p<0.05$) when all subjects are pooled and approaches statistical significance when the alcoholics are considered alone ($r = -.33$).

Given the marked heterogeneity in the proportions of smokers and nonsmokers in the two subject groups, it was not possible to conduct analyses using daily cigarette consumption as a covariate. Thus, to provide a conservative estimate of the effect of drinking on olfaction without the confound of smoking, we conducted analyses of only those subjects in each group who reported that they did not currently smoke (N = 11 and 16 in the alcoholic and control groups, respectively). *t*-Tests revealed that these two groups did not differ significantly in terms of age or years of education. The groups did, however, differ significantly on UPSIT scores ($p<0.02$); the groups means were 35.9 (SD = 2.6) and 37.8 (SD = 2.6) in the alcoholic and control groups, respectively. In addition, as shown in Fig. 2, 3 of 11 alcoholics received scores that fell into the clinically impaired range, while none of the controls received this classification. A chi-square test revealed that this difference in the incidence of clinical impairment was statistically significant ($p<0.03$). Thus, it appears that alcoholism is associated with diminished olfactory performance even when smoking history is controlled.

*MR Analyses*

Table 3 shows the MR-derived mean ventricular and cortical sulcal CSF volumes for the alcoholic and nonalcoholic subjects. Since these MR measures are expressed as age-corrected Z-scores (16), positive and negative scores indicate increments and decrements respectively in CSF volume relative to the mean for a large sample of normal controls. The difference between the alcoholic and nonalcoholic subjects on the cortical sulcal volume measure was significant ($p<0.001$), whereas the difference between the groups' ventricular volume measures only approached significance ($p<0.10$).

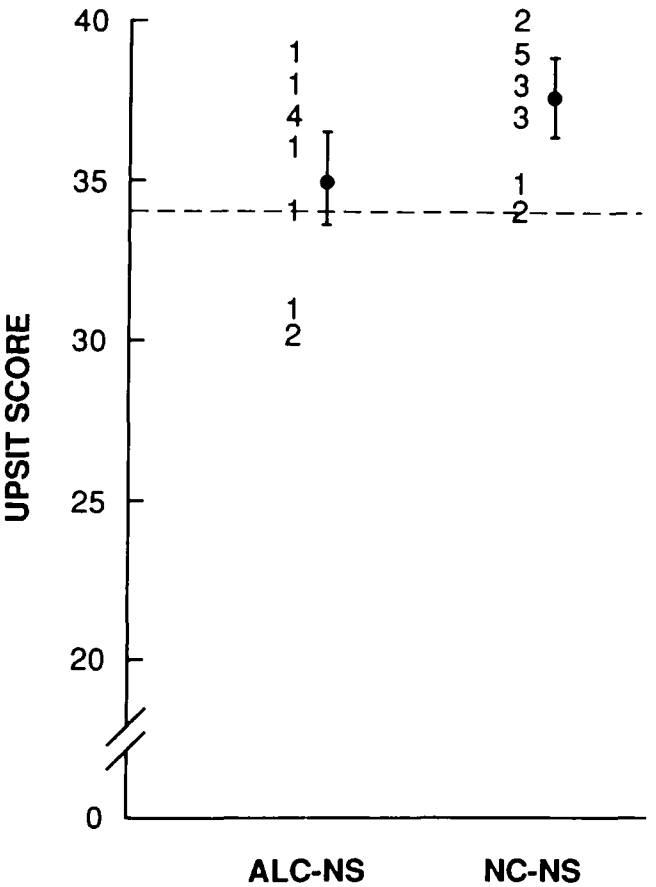


FIG. 2. Frequency distributions of UPSIT scores for alcoholics (N = 11) and nonalcoholics (N = 16) who were not currently smoking. The horizontal line drawn at 34 separates those subjects with normal scores from those with clinically significant olfactory deficits. Numerals refer to the number of individuals within each groups obtaining a given score. Vertical bars to the right of the numbers indicate the 95% confidence levels. The black dots note the mean UPSIT score for each group.

Pearson product moment correlations between baseline UPSIT scores and the ventricular and sulcal CSF volumes of the alcoholics yielded significant results. The UPSIT scores correlated −.476 ($p = 0.005$) with sulcal volumes and −.277 ($p<0.08$) with ventricular volumes derived from MRI. The correlation between the alcoholics' ventricular and sulcal volumes was significant ($r = .652$, $p<0.001$).

TABLE 3

MEAN (SD) AGE-CORRECTED Z-SCORES OF MR-DERIVED VENTRICULAR AND CORTICAL SULCAL FLUID MEASURES FOR ALCOHOLICS AND NONALCOHOLIC CONTROLS

| | Alcoholics (N = 28) | Normal Controls (N = 15) |
|---|---|---|
| Ventricular Volume | 0.981(1.741) | 0.227(1.650) |
| Cortical Sulcal Volume | 1.699(1.655) | −0.108(0.946) |

TABLE 4

MEAN (SD) UPSIT SCORES OF ALCOHOLIC AND CONTROL SUBJECTS WHO RETURNED FOR FOLLOW-UP EVALUATION

| Alcoholics (N = 23) | | Controls (N = 14) | |
|---|---|---|---|
| Baseline | Follow-Up | Baseline | Follow-Up |
| 32.7 (5.2) | 32.0 (8.2) | 37.8 (2.1) | 37.2 (2.9) |

Similar analyses for the 15 nonalcoholic controls did not result in significant correlations between fluid measures and UPSIT scores (cortical sulcal volumes = .169; $p = 0.27$; ventricular volumes = −.326; $p = 0.11$). Since the nonalcoholic controls made relatively few errors on the UPSIT, these insignificant correlations may be related to ceiling effects. Also, ventricular and sulcal volumes were not significantly correlated ($r = -.135$, $p > 0.10$) for the nonalcoholic controls. No correlation is expected in normal subjects, since the only factor likely to mediate such an association, namely age, has been removed from both measures.

*Olfactory Function at Follow-Up*

Twenty-three of the 37 alcoholics and 14 of the 21 control subjects tested at baseline were administered the UPSIT a second time at least three months later. Nine of the alcoholics and six of the controls were not scheduled for follow-up olfactory testing because their unusable MR scans at baseline made them ineligible for another study concerned with 12-month longitudinal changes in MRI and cognition. Only 5 of 28 alcoholics and 1 of 15 control subjects failed to keep their scheduled follow-up appointments. A two-sample unpaired *t*-test (two-tail) comparing the baseline UPSIT scores of those alcoholics who returned for follow-up (Mean = 33, SD = 5.8) with those alcoholics who did not return (Mean = 37, SD = 3.0) showed that those alcoholics who did return performed significantly worse ($p < 0.03$) at baseline. These two groups did not differ on any other demographical, neuropsychological or drinking history variable at time of admission.

A two-factor (group × administration date) repeated measure analysis of variance comparing UPSIT scores of alcoholics and controls at baseline and follow-up showed a significant main effect of group, $F(1,35) = 7.58$, $p < 0.009$, but not for administration date ($p < 0.28$) or the group by administration date interaction ($p < 0.89$). Thus, alcoholics consistently performed worse than controls over time (Table 4), and there is no indication that the UPSIT scores at follow-up were influenced by practice effects (i.e., lack of significant difference in the nonalcoholics' performances at baseline and follow-up).

In order to determine whether abstinence had an effect on follow-up odor identification, the alcoholic group was divided into those who remained abstinent during the period between discharge from the ATP and follow-up (N = 15) and those who did not remain abstinent during this time (N = 8). The mean age, education, drinking histories, and baseline neuropsychological test scores of the abstinent and nonabstinent alcoholics are presented in Table 5. The two groups were not significantly different on any demographical, neuropsychological or drinking history variable at admission.

A two-factor (group × administration date) repeated measures analysis of variance comparing UPSIT scores of abstinent and nonabstinent alcoholics at baseline and follow-up yielded an insignificant but definite trend in both group effect, $F(1,21) = 3.72$, $p < 0.068$, and group by administration date interaction, $F(1,21) = 4.07$, $p < 0.057$ (Fig. 3). Since the interaction of group × administration date approached significance, post hoc *t*-tests were performed. These tests revealed that alcoholics who returned to drinking performed significantly worse on the UPSIT at follow-up testing than did those alcoholics who remained abstinent ($p < 0.04$), but there was no significant difference between the groups on their baseline UPSIT scores ($p < 0.17$). In addition, there were no significant intragroup differences between baseline and follow-up UPSIT scores for either abstinent ($p < 0.83$) or nonabstinent ($p < 0.37$) alcoholics. Comparisons at follow-up of the abstinent and nonabstinent alcoholics with the nonalcoholic controls (Table 4) indicated that the nonabstinent alcoholics remained significantly impaired on the UPSIT ($p < 0.0006$), whereas the difference between those who remained abstinent (34.5) and the control subjects (37.2) did not reach statistical significance ($p < 0.19$).

TABLE 5

MEAN AGE, EDUCATION, DRINKING VARIABLES, AND NEUROPSYCHOLOGICAL TEST SCORES FOR ABSTINENT (N = 15) AND NONABSTINENT (N = 8) ALCOHOLIC SUBJECTS AT ADMISSION

| | Abstinent | Nonabstinent | $p^*$ |
|---|---|---|---|
| Age (Years) | 50.5(10.0) | 51.4(9.5) | NS |
| Education (Years) | 14.0(2.0) | 14.4(1.8) | NS |
| Years of Alcoholism | 11.4(8.3) | 13.1(11.6) | NS |
| Daily Ethanol Consumption (average number drinks per day) in 3 months prior to admission | 17.2(10.4) | 11.3(7.2) | NS |
| Vocabulary (WAIS-R Scaled Score) | 9.6(2.5) | 9.9(1.6) | NS |
| Trails A (Seconds) | 27.7(9.3) | 35.4(9.6) | NS |
| Trails B (Seconds) | 102.7(29.1) | 124.5(77.7) | NS |
| Digit Symbol (WAIS Scaled Score | 9.3(2.0) | 8.3(1.5) | NS |

*All variables were assessed with two-tailed *t*-tests.

## DISCUSSION

The present findings confirm a previous report of olfactory deficits in nonamnesic alcoholics. Besides having heightened olfactory thresholds (29), alcoholics are impaired in their ability to identify qualitatively distinct odorants. At both baseline and follow-up evaluations, the alcoholics made significantly more errors on the UPSIT than did the nonalcoholic controls. Also, using the standardized UPSIT norms more than 30% of the alcoholics, in comparison to only 5% of the nonalcoholic controls, fell into the clinically impaired range with regard to olfactory identification. Although the present results and those of Potter and Butters (29) conflict with other studies which have reported comparable olfactory performances for alcoholics and nonalcoholic control subjects (13, 20–22), these negative results may have been due to small sample sizes, methodological differences, the employment of nonstandardized tests, and a failure to choose enough odorants sensitive to the alcoholics' deficits (7,29). It is also important to note that the present findings cannot be attributed totally to differences in smoking patterns. The number of cigarettes consumed on a daily basis was negatively correlated with UPSIT scores, but comparisons limited to nonsmoking alcoholic and nonalcoholic

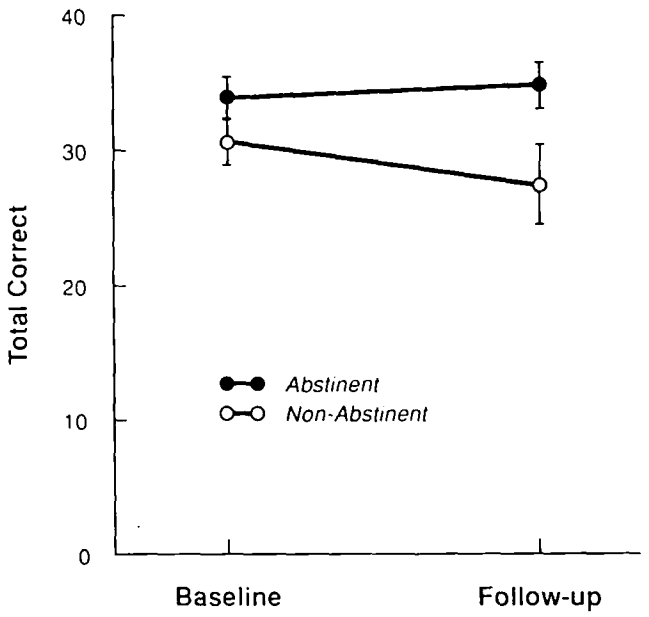


FIG. 3. Mean (SD) performance on the UPSIT of Abstinent (N = 15) and Nonabstinent (N = 8) alcoholics at Baseline and at Follow-up testing.

subjects still yielded significant group differences in olfactory identification.

The results of the correlational analyses indicate that the olfactory deficits of the alcoholics are unlikely to be due to a general cognitive disability. As expected, the alcoholics were impaired on several cognitive measures, but these cognitive deficiencies did not correlate with the patients' olfactory scores. However, since the brief neuropsychological battery and the UPSIT were administered to the alcoholics two weeks apart (i.e., at the beginning and end of their stay on the ATP, respectively), some caution must be observed in interpreting these negative findings. Perhaps some general behavioral recovery occurring during the intervening two-week period may have confounded and ultimately reduced correlations that would have been apparent if the UPSIT and the cognitive tests had been administered at the same time during the treatment program. Yet, it should be noted that the present failure to find significant correlations between UPSIT and cognitive scores are consistent with Jones-Gotman and Zattore's (23) report that olfactory and general cognitive indices are unrelated in patients with frontal, temporal, and parietal lobe damage.

The results of this study also provide some initial clues as to the effect of abstinence on olfactory functioning. Detoxified alcoholics who had significant olfactory impairments several weeks after their last drink did not evidence significant improvement after three months of abstinence. However, for those alcoholics who returned to drinking during this time period, there was a tendency to decline further in olfactory identification. It appears then that long-term alcoholism may have both a chronic and an acute effect on patients' olfactory functioning. While long-term alcohol abuse may lead to a slow, perhaps irreversible, deterioration of olfaction, alcohol may also have an acute detrimental effect which is reversible with detoxification. Since our patients were relatively few in number and were followed for only three months, some caution should be observed in drawing conclusions about the irreversibility of the seemingly chronic olfactory impairments. Such circumspection seems especially warranted given that full recovery of some cognitive functions may require more than five years of continual abstinence (4, 9, 11, 12).

While some neuroradiological studies have associated alcoholics' cognitive deficits with specific cortical and/or subcortical changes (1, 2, 10, 41), the present study represents the first attempt at such brain-behavior analyses of these patients' olfactory impairments. Based upon the established neuroanatomical circuits underlying olfaction (26, 31, 37, 38), damage to the medial diencephalon, the anterior portions of the temporal lobes and/or orbitofrontal cortex would seem the most likely neurologic basis of the alcoholics' deficiencies in odor identification. Both Jones and her colleagues (20–22) and Potter and Butters (29) emphasized the role of diencephalic structures in the olfactory problems of amnesic and nonamnesic alcoholics, but demonstrations (23,30) that damage to the orbital frontal and temporal cortices result in severe deficits on the UPSIT suggest that alcoholics' impairments in odor identification may be related to cortical rather than to subcortical factors. The present findings of a highly significant moderate correlation between cortical sulcal volumes and UPSIT scores would seem to provide further support for the cortical basis of these olfactory deficiencies. However, since the correlation between ventricular volume and odor identification also approached significance, the role of subcortical diencephalic structures cannot be totally dismissed. Given that long-term alcoholism results in widespread cortical and subcortical changes (1–3, 14, 41), it is possible that a number of cortical and subcortical neurologic structures contribute to the olfactory impairments described in this report.

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