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The Effects of Chronic Cigarette Smoking On Cognitive Recovery During Early Abstinence from Alcohol

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Abstract

Background—Alcohol use disorders are related to neurocognitive abnormalities during early abstinence in those seeking treatment for alcohol dependence (ALC). Considerable evidence indicates that chronic cigarette smoking is associated with multiple neurocognitive deficiencies. However, very little is known about the effects of chronic smoking on neurocognitive recovery during early abstinence from alcohol. We evaluated if cigarette smoking interferes with cognitive improvement during early abstinence from alcohol, a period thought important for maintaining long-term sobriety.

Methods—Neurocognitive functions previously shown to be adversely affected by both alcohol use disorders and chronic cigarette smoking were evaluated. We assessed 35 smoking ALC (sALC) and 34 non-smoking ALC (nsALC) at approximately one and five weeks of monitored abstinence.

Results—Although neither group was clinically impaired, both cross-sectional and longitudinal deficiencies were observed in sALC vs. nsALC in processing speed, working memory and auditory-verbal learning and memory. Lifetime alcohol consumption, medical and psychiatric comorbidities did not predict neurocognitive performance or improvement across assessments. Within sALC, greater drinking and smoking severities were synergistically (more than additively) related to less improvement on visuospatial learning and memory. Former smoking status in the nsALC group mediated group differences in auditory-verbal delayed recall.

Conclusions—Chronic cigarette smoking appears to negatively impact neurocognition during early abstinence from alcohol. Although the cognitive deficiencies observed in this cohort were not in a clinical range of impairment, they should be considered. Our findings lend support to integrating smoking cessation as well as the individual assessment of cognition into early alcohol dependence treatment. Additionally, there is a need to elucidate the effects of current and former smoking status in future reports of neurocognition.

Keywords

alcohol dependence; cigarette smoking; cognition; treatment; former smoking

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INTRODUCTION

Although smoking rates in the general population have declined in the United States over the last decade, chronic cigarette smoking is common among those with Axis I and II disorders (Grant et al., 2004), with smoking rates for individuals with an alcohol use disorder (i.e., alcohol abuse or dependence) ranging from 60–90% (Durazzo et al., 2007a; Hurt et al., 1994; Kalman et al., 2005; Le, 2002; Romberger and Grant, 2004). There is increasing evidence that the combination of chronic cigarette smoking and alcohol use disorders has significant adverse effects on both neurocognition and brain biology (Durazzo et al., 2007a; 2010a), reminiscent of the increased risks for oropharygeal cancer and ill-effects on general health posed by the combination of chronic smoking and excessive alcohol consumption (Kalman et al., 2010). Few studies, however, have assessed the combined effects of cigarette and alcohol consumption on neurocognition in alcohol use disorders, even though cognitive functioning may influence integration of treatment interventions and treatment outcome during early sobriety (Bates et al., 2006; Cunha and Novaes, 2004).

In the few published cross-sectional studies that evaluated the combined effects of chronic smoking and alcohol use disorders within the first 90 days of abstinence from alcohol, both chronicity of alcohol misuse and cigarette smoking were inversely related to measures of general intellectual functioning, set-shifting and processing speed (Friend et al., 2005). Treatment-seeking alcohol dependent (ALC) smokers at three months of abstinence performed significantly worse on measures of verbal intelligence than age- and education-equivalent non-smokers (Rosenbloom et al., 2005). ALC smokers with approximately six weeks of abstinence, were administered a high and low dose of nicotine. Interestingly, a higher dose was related to greater accuracy on a working memory task than a lower dose; however, irrespective of dose, greater pack years was related to longer reaction times and lower accuracy on the same task (Boissoneault et al., 2011). In community-based samples with alcohol dependence, higher pack-years were inversely related to measures of cognitive proficiency and general intelligence (Glass et al., 2006), and both alcohol and smoking severities were inversely related to executive function (Glass et al., 2009). A series of cross-sectional studies in treatment-seeking ALC at one month of abstinence from alcohol showed worse cognitive performance in smoking ALC (sALC) than non-smoking ALC (nsALC) on measures of auditory-verbal learning and memory, processing speed, cognitive efficiency, and static postural stability (Durazzo et al., 2006; 2008; 2010a).

Even fewer studies have examined the effects of continued cigarette smoking on neurocognitive recovery during early abstinence from alcohol in treatment-seeking individuals. In treatment-seeking ALC, we examined neurocognitive changes between *one month and six to nine* months of abstinence (Durazzo et al., 2007b): nsALC exhibited significantly greater longitudinal improvements than sALC on measures of cognitive efficiency, executive skills, visuospatial skills, and working memory after controlling for age, education, estimated premorbid verbal IQ, and alcohol consumption. In addition, smoking severity was inversely related to longitudinal improvement on multiple cognitive measures, suggesting that cumulative adverse neurobiological effects of chronic smoking (Durazzo et al., 2007; 2010b) modulate cognitive recovery with extended abstinence from alcohol.

The early weeks after alcohol cessation, once any acute withdrawal symptoms have subsided, are a critical time for sustaining abstinence and engaging in treatment (Bates et al., 2006; Cunha and Novaes, 2004). Given the significant adverse effects of chronic smoking in non-clinical populations (Durazzo et al., 2010b), the scant neurocognitive findings in recently abstinent ALC reviewed above, and our lack of knowledge on smoking effects on

neurocognitive change during early abstinence, the main goals of this study were to determine the degree to which: a) smoking status and severity in treatment seeking ALC influence cognitive performance at one week of sobriety, and b) chronic smoking moderates cognitive changes between one and five weeks of abstinence from alcohol. Specifically, we predicted that:

1. At one week of abstinence from alcohol, nsALC perform superior to sALC on specific measures assessing auditory-verbal/visual-spatial learning and memory, working memory, and processing speed.
2. Between one and five weeks of abstinence, nsALC show a greater magnitude of neurocognitive improvement than sALC on these same measures.
3. Within sALC, lifetime years of smoking and average alcoholic drinks per month over lifetime modulate short-term cognitive change, i.e., greater smoking and past drinking severities are associated with less cognitive improvement over one month of early abstinence.

METHODS

Participants

Treatment seeking alcohol dependent patients (ALC) were recruited from outpatient clinics of the VA Medical Center and Kaiser Permanente in San Francisco, CA. Prior to study, all participants gave written informed consent, which had been approved by research review boards of the University of California San Francisco and the San Francisco VA Medical Center. At the time of enrollment, all participants were between the ages of 28 and 71. Sixty-nine nsALC (n=34) and sALC (n=35) completed neuropsychological assessment after 6 ± 3 days of abstinence from alcohol (TP1) and were re-evaluated after 35 ± 9 days of abstinence from alcohol (TP2). The number of days abstinent at TP1 and TP2 were equivalent for both groups.

Primary inclusion criteria for ALC were current DSM-IV diagnosis of alcohol dependence or abuse (American Psychiatric Association, 1994), fluency in English, consumption of >150 alcoholic drinks per month (1 alcoholic drink equivalent = 13.6 g pure alcohol) for at least 8 years before enrollment for men, and consumption of >80 drinks per month for at least 6 years before enrollment for women. All met DSM-IV criteria for alcohol dependence, 90% with physiological dependence. Primary exclusion criteria are fully detailed in Durazzo et al. (2004). In summary, all participants were free of general medical, neurologic, and psychiatric conditions known or suspected to influence neurocognition, except for hepatitis C, hypertension, and unipolar mood disorders. Current or past unipolar mood disorders (e.g., major depression, substance-induced mood disorder) were not exclusionary, given the high comorbidity with both alcohol use disorder (Gilman and Abraham, 2001) and chronic cigarette smoking (Fergusson et al., 2003; Paperwalla et al., 2004). Dependence within five years of study on any drug other than alcohol or nicotine was exclusionary. All participants were screened for recent use of common illicit substances and tested for recent alcohol consumption (both urine and breath). No participant was positive for alcohol or other substances at TP1 or TP2, and no participant reported or tested positive for alcohol or substance use between assessments.

Psychiatric/Behavioral Assessment

At TP1, ALC participants completed the Structured Clinical Interview for DSM-IV Axis I disorders, Patient Edition, Version 2.0 [SCID-I/P; (American Psychiatric Association, 1994)] and standardized questionnaires assessing depressive [Beck Depression Inventory (BDI); (Beck, 1978)] and anxiety symptomatologies [State-Trait Anxiety Inventory form

Y-2 (STAI); (Spielberger et al., 1977)], lifetime alcohol consumption [Lifetime Drinking History; (Skinner and Sheu, 1982)] and lifetime substance use (in-house questionnaire assessing quantity and frequency of any substance use), and current level of nicotine dependence (Fagerstrom Tolerance Test for Nicotine Dependence, FTND;(Fagerstrom et al., 1991). The average number of alcoholic drinks per month were calculated for 1 year before study, average number of drinks per month over a lifetime, number of years of regular drinking (i.e., consuming at least one alcoholic drink per month), number of months of heavy drinking (i.e., drinking in excess of 100 (80 for females) drinks per month), and age of onset of heavy drinking. At both assessment points, the total number of cigarettes smoked per day and number of years of smoking at the current level were recorded for sALC participants.

Laboratory Tests

γ-Glutamyltransferase (GGT, a marker of recent heavy alcohol consumption (Sillanaukee et al., 2000), prealbumin and complete blood count (proxies for nutritional status (Weinrebe et al., 2002), liver function panels, as well as common electrolytes were obtained at both assessments.

Neurocognitive Assessment

Neuropsychological testing (approximately 1.5 hours) evaluated cognitive functions known to be adversely affected by both alcohol dependence (Rourke and Grant, 2009) and chronic cigarette smoking (Durazzo et al., 2010b). Alternate forms were used where available for TP2. The plasma half-life of nicotine is about 2 hours (Nakajima and Yokoi, 2005). Therefore, smoking ALC were allowed to smoke *ad libitum* before and during neurocognitive testing to reduce potential confounds of nicotine withdrawal (for review see Sacco et al., 2004). The following tests were administered: Wechsler Adult Intelligence Scale 3rded. (WAIS-III) (Wechsler, 1997) - Digit Span (working memory), Symbol Search, and Digit Symbol (processing speed); California Verbal Learning Test-II (CVLT-II) (Delis et al., 2000) - Immediate Recall trials 1 to 5 (auditory-verbal learning), Short and Long Delay Free Recall (auditory-verbal memory); Brief Visual Memory Test (BVMT) Revised (Benedict, 1997) - Total Recall (visuospatial learning) and Delayed Recall (visuospatial memory). Premorbid verbal intelligence was assessed using the American National Adult Reading Test (AMNART) (Grober and Sliwinski, 1991). Raw scores for all neurocognitive measures were converted to standardized scores via appropriate normative data adjusted for age.

Data Analyses

Cross-sectional—Multivariate analysis of covariance (MANCOVA) assessed differences between sALC and nsALC at both assessments. At TP1, a smaller cohort of 17 sALC and 21nsALC (55% of entire sample) completed four of the eight tests included in the battery (WAIS-III Symbol Search, CVLT-II learning, Short Free Recall, and Long Free Recall). This sub-sample was analyzed separately. All participants completed the full battery of eight tests at TP2. All cross-sectional comparisons were covaried for depressive symptomatology (BDI), estimated premorbid verbal intelligence (AMNART), lifetime average monthly alcoholic drinks, as were all significant follow up pairwise comparisons. Despite using age corrected norms, age was a significant predictor of neurocognition in our previous studies with this cohort (Durazzo et al., 2008); therefore, age was used as a covariate. The standard alpha level (0.05) for main effects and follow up pairwise comparisons were adjusted for multiple comparisons using a modified Bonferroni method (Sankoh et al., 1997). This approach considers the mean correlation between variables and the number of tests in the adjustment of alpha levels. Therefore, we summed the intercorrelations among all

neurocognitive measures and divided the result by the number of correlations used (average r = 0.42). This correlation along with the eight tests was used to derive an adjusted alpha level of $p \leq .015$. Effects sizes (ES) were calculated using Cohen's *d* (Cohen, 1988). All statistical analyses were conducted with SPSS v19.

Longitudinal—Longitudinal neurocognitive change for sALC and nsALC between TP1 and TP2 was compared with linear mixed modeling and paired t-tests (2-tailed), using the same covariates as the cross-sectional analyses. Interactions, main effects and follow-up paired t-tests were corrected for multiple comparisons as described above (adjusted $p \leq .015$). To compute percent change, all standardized scores were converted to t-scores and then calculated as [(t-score at TP2 - t-score at TP1)/t-score at TP1)*100].

RESULTS

Participant Characterization (See Table 1)

Of the 69 ALC participants (8 female), 52 were Caucasian, 10 were African American, three Latino, three Native American and one was Polynesian/Pacific Islander. The data obtained from female participants fell within the overall ranges of scores and did not contribute to the variance on any measure. nsALC and sALC were equivalent on age and AMNART score; nsALC tended to have more years of education (p = .06). sALC relative to nsALC consumed more alcoholic drinks per month over 1 year (+33%, p = .04) before enrollment and over lifetime (+62%, p < .01). Although the groups did not differ on total lifetime years drinking, sALC began drinking heavily (i.e., >100 drinks per month) at a significantly younger age than nsALC (22 vs. 31 years of age, p < .01). At enrollment, 9/34 nsALC and 4/35 sALC participants met DSM-IV criteria for recurrent major depression and seven nsALC and four sALC for substance-induced (alcohol) mood disorder with depressive features. However, the groups did not differ on the proportion of comorbid recurrent major depression (p = .13) and alcohol induced mood disorder (p = .96). At TP2, two nsALC and one sALC continued to have substance-induced (alcohol) mood disorder with depressive features, and all participants who met criteria for recurrent major depression at TP1 continued to meet criteria at TP2.

One sALC and two nsALC participants met criteria for cocaine abuse at TP1, and all were in early full remission at TP2. Nine of 34 nsALC and 9/35 sALC had medically controlled hypertension, and 4/34 nsALC and 11/35 sALC were positive for the hepatitis C antibody. The proportion of hypertension (p = .94) and hepatitis C (p = .16) were equivalent in both groups, and neither contributed to variance on any measure. The groups were not significantly different on the BDI, STAI, or on any of the clinical laboratory variables. All sALC were actively smoking at both TPs with no significant change in cigarette consumption between assessments. At TP1, the average sALC FTND score was 5.5 ± 1.9 (moderate to high level of nicotine dependence) and they smoked 20 ± 8 cigarettes per day. At TP2, the average FTND score and average daily cigarette use were virtually identical to TP1.

Cross-Sectional Findings at TP1

The omnibus MANCOVA (covaried for age and AMNART) comparing nsALC and sALC on BVMT learning, BVMT Delayed Recall, WAIS-III Digit Span, and WAIS-III Digit Symbol was not significant [F (4,61) = 1.85, p= .131]. The omnibus MANCOVA comparing the subgroups, who received the shortened battery of measures (WAIS-III Symbol Search, CVLT-II learning, Short Free Recall and Long Free Recall) at TP1, revealed a trend [F (4, 33) = 2.23 p = .087] for superior performance by nsALC. Planned pairwise comparisons, however, showed nsALC superior to sALC on Digit Symbol (p = .012, ES = .57) and

Symbol Search (p = .005, ES = .89), with moderate and strong effect sizes. nsALC tended to perform better than sALC on both BVMT learning (p = .089, ES = .34) and Delayed Recall (p = .082, ES = .35), with weak effect sizes for both measures. nsALC also tended to do better on CVLT learning, Short Free Recall and Long Free Recall with moderate effect sizes (p = .023 – .057, ES = .53 – .68). Higher AMNART scores predicted better performance on Digit Span, Symbol Search, and BVMT Learning (all p < .015), while increasing age predicted worse BVMT Learning (p = .006).

Longitudinal Findings (See Table 2)

We predicted less improvement across measures in sALC compared to nsALC over four weeks of sobriety between assessments. However, a statistical trend for a smoking status-by-TP interaction was seen only for CVLT Long Free Recall [F (1, 44) = 2.98, p = .091]. Follow-up paired t-tests indicated that sALC demonstrated a significant *decrease* in performance across time (p = .014), whereas nsALC showed no significant change (p = .665). Main effects for TP were seen for Digit Symbol [F (1, 59) = 6.62, p = .013], Symbol Search [F (1, 49) = 17.50, p < .001], and BVMT Learning [F (1, 70) = 37, p < .001]. Paired t-tests revealed that both sALC and nsALC showed equivalent improvements across TPs for these three measures (all p <. 009). Digit Span showed a trend for a main effect of time [F (1, 77) = 3.72, p = .057], with nsALC improving significantly (p = .013) and sALC showing no change. Main effects and follow up t-tests for BVMT Delayed Recall, CVLT Learning and CVLT Short Free Recall were not significant, indicating that neither sALC nor nsALC demonstrated significant change across TPs on these measures. Higher AMNART scores predicted greater improvements on Digit Span, Digit Symbol, Symbol Search, BVMT Learning and Recall, and CVLT Learning (all p < .015). Greater age was related to less improvement on Digit Span, Symbol Search, and BVMT Learning and Recall (all p < .015). Higher BDI was associated with less improvement on Digit Symbol (p = .003).

Cross-Sectional Findings at TP2

The omnibus MANCOVA (covaried for age and AMNART) comparing nsALC and sALC on all measures at TP2 revealed a trend for group differences [F (8, 54) = 1.89, p = .080]. However, in planned comparisons, nsALC were superior to sALC on Digit Symbol, CVLT-II learning and CVLT Long Free Recall (p = .005 – .011; ES = .59 – .67). nsALC also tended to perform better than sALC on Symbol Search (p = .078; ES = .36) and CVLT-II Short Free Recall (p = .10; ES = .32). Higher AMNART scores predicted better performance on Digit Span, Digit Symbol, and Symbol Search (all p < .015); and greater age was related to worse TP2 performance on Digit Span, Symbol Search, BVMT Learning and Recall (all p < .015).

Relationship of Combined Smoking and Drinking Severities on Cognitive Recovery in sALC

In sALC, the interaction of lifetime years smoking-by-average alcoholic drinks per month over the lifetime was a significant predictor of change between TP1 and TP2 for BVMT Learning (Learning (β = −.003, standard error (SE) = .001, p = .008) and Delayed Recall (β = −.003, SE = .001, p = .011) after controlling for days sober. For these measures, greater drinking and smoking severities were synergistically (more than additively) related to less improvement in sALC across the assessment interval.

Former vs. Never Smoking ALC

Individuals who quit smoking in the past perform intermediate to never and active smokers on several neurocognitive tests (Ernst and al., 2001; Fried et al., 2006; Starr et al., 2007); therefore, we conducted follow-up analyses in our currently non-smoking ALC group,

comparing 21 never smokers (62%) to 13 former smokers on all significant findings. Former smokers reported consuming at least 8 cigarettes a week for at least one year during their lifetime, and were smoke-free for an average of 10 ± 9 years (range: 1 – 30 years) before the study. On CVLT-II Long Free Recall at TP2, former smokers performed significantly worse than never smokers (mean z-score = 0.04 ± .90 vs. 1.03 ± 1.03, p=.004). When former smokers were removed from the nsALC group, TP2 differences between never smokers and sALC (mean z-score difference = 0.99) on CVLT-II Long Free Recall remained significant (p<.001), and the effect size increased from moderate (d = .66) to strong (d = 1.19). When former smokers were removed from longitudinal analyses, CVLT-II Long Free Recall continued to show a trend for a smoking-by-TP interaction [F (1, 31) = 2.95, p = .096]; pairwise t-tests (2-tailed) indicated that sALC demonstrated a significant *decrease* in CVLT-II Long Free Recall across time [(1, 23) F = 7.01, p = .014], whereas never smokers showed no change [F (1, 11) = 0.23, p = .639].

DISCUSSION

As predicted, in this abstinent alcohol dependent cohort, nsALC performed better than sALC on measures of processing speed (Digit Symbol and Symbol Search) at one week of abstinence and on processing speed (Digit Symbol only) and on auditory-verbal learning and memory (delayed recall) at five weeks of abstinence from alcohol. The five-week findings were consistent with our previous reports (Durazzo et al., 2006; 2008; 2010a) in a similar cohort. nsALC improved significantly between one and five weeks of abstinence from alcohol on working memory (Digit Span), while both groups showed equivalent longitudinal improvements on processing speed and visuospatial learning. Unexpectedly, sALC exhibited a decline on auditory-verbal delayed recall during this early abstinence period, whereas nsALC remained stable. Greater lifetime alcohol consumption and age of onset of heavy drinking were not related to performance on any domain in either group. This is consistent with other studies (Beatty et al., 1995; 2000; Eckardt et al., 1998; Horner et al., 1999; Schafer et al., 1991; Sullivan et al., 2000) and our previous longitudinal report (Durazzo et al., 2007b) that indicated measures of alcohol consumption quantity/frequency were weakly or not significantly related to neurocognition. Past substance use disorders, and psychiatric and medical comorbidities were also not associated with *changes* on any cognitive domain. Older age (despite the use of age-adjusted norms) and lower AMNART scores predicted worse performance on several cross-sectional and longitudinal tests in both ALC groups. We posit that the observed cognitive differences between nsALC and sALC during early abstinence from alcohol may impact both clinical and research considerations.

Clinical Considerations

Reports show that 45% of alcohol dependent patients have no clinical neurocognitive impairment after 2–3 weeks of abstinence (Grant and Adams, 2009). Consistent with this, we found no clinical impairment (i.e., ≥ 1.5 SD or ≤ 7th %ile) in either sALC or nsALC at the group level at one or five weeks of abstinence from alcohol: both nsALC and sALC had intact processing speed, working memory and auditory-verbal/visuospatial learning and memory and, thus, likely possessed many of the requisite cognitive functions to benefit from traditional methods of addiction treatment (e.g., cognitive behavioral therapy, motivational enhancement therapy, etc) in the weeks immediately following abstinence from alcohol. Nevertheless, there is a wide range of cognitive performance across the groups, and specific consideration of the different patterns of cognitive performance between sALC vs. nsALC may help maximize the benefits from cognitively demanding treatment approaches. Specifically, the group differences in working memory, processing speed, auditory-verbal learning and delayed recall, in addition to the synergistic effect of smoking and alcohol consumption on visual spatial learning and recall, suggest that sALC, although not impaired,

may need more time and/or targeted acute treatment during early abstinence to achieve maximal recovery from alcohol dependence. Although reports on the predictive ability of neuropsychological functioning in treatment outcome can be contradictory (Adamson et al., 2009; Donovan et al., 1984), some have shown that cognitive functioning influences the efficacy of treatment interventions and treatment outcome during early sobriety (Bates et al., 2006; Cunha and Novaes, 2004). Treatment providers may increase individual treatment efficacy/outcome by considering their patients' cognitive performance along with estimated premorbid verbal intelligence, age and other salient variables such as personality traits and environmental factors. For example, these group differences together with the results of individual cognitive assessments could inform compensational and cognitive remediation techniques aimed at optimizing individual recovery. Finally, although speculative, smoking cessation is expected to enhance cognitive recovery during abstinence from alcohol. When integrating smoking cessation into substance use disorder treatment programs (Kalman et al., 2010), the nature of the specific cognitive deficiencies in sALC may be worth considering as well.

Consideration of Former Smoking Status in ALC

Following up on reports that former smokers generally perform intermediate to never and current smokers (Ernst and al., 2001; Fried et al., 2006; Starr et al., 2007), we showed that former smoking ALC (i.e., those who stopped smoking between one and 30 years ago and were smoke-free for an average of 10 years) performed worse than never smoking ALC on auditory-verbal delayed recall at five weeks of abstinence from alcohol. Consequently, removing former smoking ALC from our analyses increased effect sizes between nsALC and sALC. Problems in auditory-verbal delayed recall in former smokers may either persist over an average of 10 years, be influenced by comorbid or premorbid factors not assessed in this study, or both. Irrespective, former smoking status modulates neurocognition and may have affected auditory-verbal delayed recall and/or other domains of neurocognition reported in the literature. In fact, the effect sizes for differences in auditory-verbal learning and recall between our never-smoking ALC and sALC are often stronger than those seen in a recent meta-analysis that examined cognition between controls and ALC with less than 1 month of abstinence and without smoking status stratification (Stavro et al., 2012). These findings suggest that it is important to consider both current and former smoking status in both ALC and control groups to better understand all contributors to the considerable range of neurocognitive abilities demonstrated in clinical and research cohorts.

Limitations

Although we statistically controlled for factors that may have influenced our dependent measures (education, premorbid intellectual functioning, drinking severity), it is possible that performance was influenced by potential unrecorded group differences in nutrition, exercise, overall physical health, exposure to environmental cigarette smoke and comorbid or premorbid conditions. Our test battery tapped specific cognitive domains and there are limits to generalizing our findings to domains assessed with a larger range of individual measures. Additionally, we had a subsample at TP1 which only received 4 of our tests; thus, replication with a larger sample early in treatment in addition to a more comprehensive cognitive assessment is desirable. We also did not include a light-drinking control population for comparison to determine if similar cross-sectional smoking effects were present in non-alcoholic populations (but see (Durazzo et al., 2012) on effects of smoking on cognition in non-clinical populations). Finally, the majority of our study participants were Caucasian males recruited from the San Francisco VA Medical Center, reflecting the veteran population; this did not allow assessment of gender or ethnicity effects on our outcome measures. Nevertheless, the overall results reveal measurable differential cognitive abilities as a function of smoking status in recently abstinent alcohol dependent individuals.

Conclusions

To our knowledge, this is the first study that examined the combined effects of lifetime alcohol consumption and cigarette smoking on neurocognitive changes during the first few weeks of abstinence from alcohol. This early abstinence period is of critical importance for active treatment engagement, when integration of treatment components would arguably be facilitated by greater cognitive acuity. The data also complement our report of greater improvement in nsALC vs. sALC on measures of cognitive efficiency, executive skills, visuospatial skills, and working memory observed between one and eight months of abstinence (Durazzo et al., 2007b).

Although on average, our recently abstinent ALC were not clinically impaired, clinicians should be aware that sALC during early abstinence may exhibit poorer performance than their non-smoking counterparts in processing speed and auditory-verbal learning and recall, may lag in their improvement of working memory, and even show a decline in auditory-verbal delayed recall. In addition, former smoking status among alcohol dependent individuals seems to merit additional consideration in regards to performance on auditory-verbal delayed recall. Practically, these differences could be used to inform specific treatment program development and allocate additional treatment resources to those in greater need. Specifically, sALC may require longer duration of treatment and/or more acute treatment corresponding to a delay in achieving their full cognitive potential.

Additionally, our findings may help guide the development of targeted cognitive remediation techniques for alcohol dependent treatment seekers. When taken together with literature on social and neurobiological influences, it may also aid the development of other behavioral and pharmaceutical treatments for this population. Furthermore, mortality levels in treatment seeking ALC are more highly related to nicotine than alcohol dependence (Hurt et al., 1996), underscoring the great importance of successful smoking cessation treatment. Therefore, at a minimum and in agreement with the literature (e.g., Kalman et al., 2010) and our earlier recommendations (Durazzo et al., 2010a), the results of this study provide additional support for the general encouragement of smoking cessation for enhanced neurocognitive recovery during early sobriety.

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Table 1

Group Demographics, Alcohol, Cigarette and Psychiatric Histories at TP1: Mean (±SD) [min, max]

Measure	nsALC	sALC
Number of participants (female)	34 (6)	35 (2)
Number of participants in TP1 subgroup (female)	21 (6)	17 (1)
Age (years)	52.1 (10.6) [31, 70]	48.2 (8.9) [28, 63]
Education (years)	14.5 (2.3) [12, 20]	13.5 (1.9) [12, 20]
AMNART	115 (9) [95, 128]	112 (9) [91, 128]
Percent Caucasian/African American/Latino	76/15/4%	74/15/4%
Number of days abstinent at TP1	7 (4) [1, 16]	6 (3) [1, 11]
Number of days abstinent at TP2	36 (9)	34 (9)
1-yr average alcoholic drinks/month	329 (203) [60, 870]	436 (212) * [64, 1050]
Lifetime average alcoholic drinks/month	170 (122) [28, 532]	275 (120) ** [45, 543]
Onset of heavy drinking [years]	31 (14) [15, 69]	22 (6) ** [14, 50]
Duration of drinking [years]	35 (11) [10, 58]	31 (9) [11, 45]
Percent with current medical comorbidity	38%	57%
Percent with current substance abuse comorbidity	5%	3%
Percent with current psychiatric comorbidity	32%	14%
FTND	NA	5.5 (1.8) [2, 10]
Cigarettes per day	NA	19.9 (8.2) [5, 40]
Smoking duration (years)	NA	24.1 (13.2) [2, 44]
Former Smokers	13 (38%)	NA
Former Smokers in TP1 subgroup	11 (32%)	NA
Beck Depression Inventory	13.7 (9.5) [0, 36]	14.9 (9.7) [0, 38]
STAI	47.0 (11.6) [20, 61]	49.1 (12.9) [22, 57]

Note. FTND: Fagerstrom Tolerance Test for Nicotine Dependence; NA: not applicable; nsALC: non-smoking alcohol dependent participant; sALC: smoking alcohol dependent participant; BDI: Beck Depression Inventory; STAI: State-Trait Anxiety Inventory – Trait.

* $p < .05$,

** $p \leq .01$

Table 2

Neurocognitive Standard Scores (mean ± SD) by Group Across Time and Percent Change

Cognitive Test	Smoking Status	TP1 (1 week)	TP2 (5 weeks)	% Change	p-value
Digit Span	Smoker	10.49 ± 3.38	10.78 ± 3.18	+ 1.9	.132
(Scaled Score)	NonSmoker	9.89 ± 3.34	10.64 ± 3.43	+ 4.8	.013 *
Digit Symbol	Smoker	7.80 ± 3.09	8.66 ± 2.86	+ 6.3	.008 *
(Scaled Score)	NonSmoker	9.06 ± 3.06	10.38 ± 3.11	+ 8.6	.000 *
Symbol Search	Smoker	9.75 ± 2.56 &	11.00 ± 2.48	+ 7.8	.005 *
(Scaled Score)	NonSmoker	10.54 ± 2.74 &	11.41 ± 2.44	+ 5.3	.008 *
BVMT Learning	Smoker	35.14 ± 14.46	45.74 ± 14.46	+23.2	.000 *
(t-score)	NonSmoker	38.99 ± 14.17	48.57 ± 14.29	+19.7	.000 *
BVMT Delayed Recall	Smoker	38.57 ± 17.33	44.84 ± 16.73	+14.0	.147
(t-score)	NonSmoker	43.19 ± 16.94	47.47 ± 17.14	+ 9.0	.281
CVLT Learning	Smoker	53.64 ± 11.31 &	52.73 ± 11.09	− 1.7	.264
(t-score)	NonSmoker	57.95 ± 11.93 &	58.12 ± 11.40	+ 0.3	.813
CVLT Short Free Recall (z-score)	Smoker	0.33 ± 1.16 &	0.10 ± 1.11	− 4.5	.315
	NonSmoker	0.59 ± 1.20 &	0.38 ± 1.16	− 4.0	.388
CVLT Long Free Recall (z-score)	Smoker	0.48 ± 1.14 &	0.04 ± 1.10	− 8.7	.014 *
	NonSmoker	0.68 ± 1.20 &	0.64 ± 1.14	− 0.7	.665

* $p < .015$;

& subset of 21 nsALC and 17 sALC at TP1.