

**Persistent but less severe ataxia in long-term vs. short-term abstinent
alcoholic men and women: a cross-sectional analysis**

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Abstract

Background: Disturbed gait and balance are among the most consistent and salient sequelae of chronic alcoholism. Results of small sample longitudinal investigations have provided evidence that partial recovery of gait and balance functions in alcoholics may be achieved with abstinence. However, abstinence durations reported have been limited, and their power and generalizability have suffered from small sample sizes.

Methods: In the present study we employed a cross-sectional approach to assess gait and balance functions in short-term (6 to 15 weeks) abstinent (STAA; n = 70) and long-term (minimum 18 months, mean = 7.38 years) abstinent (LTAA; n = 82) alcoholics. STAA and LTAA did not differ with respect to lifetime alcohol consumption, family drinking density, or years of education. In addition, we examined effects of gender and alcohol use variables.

Results: Our main findings were 1) persistent disturbed gait and balance in STAA, and disturbed standing balance in LTAA, 2) overall less impaired performance of LTAA compared to STAA on gait and balance measures, and 3) worse performance of STAA (but not LTAA) women, compared to men, on standing balance without visual control.

Conclusions: Our results suggest that alcoholics' gait and balance can continue to recover with long abstinence from alcohol, but that deficits persist, especially in eyes-closed standing balance. In addition, our results are consistent with more severe alcohol-induced ataxia in women than in men but suggest that, with extended abstinence, women recover gait and balance function to a level comparable with men.

Key Words: alcoholics; ataxia; gait and balance; recovery; extended abstinence; cerebellum

Introduction

Upright balance and gait may be disrupted by damage to any of several neural systems. Cerebellar atrophy, typically most pronounced in the anterior superior portion of the vermis, is one of the most widely recognized structural changes in the human brain caused by long-term heavy alcohol consumption (Andersen 2004, Gilman et al. 1990, Harper 1993, Pfefferbaum and Rosenbloom 1993, Torvik and Torp 1986). Mechanisms underlying ethanol-induced neuropathology and functional alterations in the cerebellum include excitotoxicity, dietary factors (particularly, thiamine depletion), glial abnormalities, oxidative stress, and impaired energy production (Alexander-Kaufman et al. 2007, Baker et al. 1999, Jaatinen and Rintala 2008, Pentney 1993, Phillips et al. 1987, Pierce et al. 1999). Numerous lesion studies (Victor et al. 1959, 1989) and behavioral and brain imaging investigations (Gilman et al. 1990, Rosenbloom et al. 2004, 2007, Sullivan et al. 2006, 2000b, 2000c) have demonstrated a strong association between cerebellar damage and impaired gait and balance, marked by lower limb ataxia.

Other imaging studies have demonstrated alcohol-induced degradation of white matter integrity, seen as white matter hyperintensities (Fein et al. 2009) and compromised fiber integrity in the corpus callosum, measured with diffusion tensor imaging (Pfefferbaum et al. 2006). Both white matter hyperintensities (Guttman et al. 2000, Starr et al. 2003, Sullivan et al. 2009) and damage to callosal fibers (Pfefferbaum et al. 2006) have been associated with postural instability. In addition, ataxia has been associated with alcohol-related peripheral neuropathy (Melgaard and Ahlgren 1986) but see Schroth et al. (1988). Finally, imaging studies (Sullivan et al. 2005) have found reduced striatal volumes in alcoholics, and alcohol dependence is associated with blunted dopamine transmission in the ventral striatum (Martinez et al. 2005), potentially resulting in disturbed gait. Recent human positron emission tomography (PET) studies have found that

dopaminergic denervation affects gait independent of age-related changes (Cham et al. 2008), and striatal involvement in the gross movement deficits of Parkinson's disease is well recognized (Fama and Sullivan 2002, Lewis et al. 2003). Not surprisingly, disturbed gait and balance are among the most consistent and salient sequelae of chronic alcoholism (Gilman et al. 1990, Rosenbloom et al. 2004, 2007, Sullivan et al. 2000a, 2000b, 2000c).

Several investigations have explored the degree to which recovery of gait and balance functions in alcoholics may be achieved with abstinence from alcohol. For example, in a study of postural stability in alcoholics who presented with clinical signs of cerebellar atrophy of the anterior lobe (Diener et al. 1984), 11 alcoholics who maintained sobriety for an average of 18.5 months after initial testing exhibited a significant decrease of body sway, whereas six alcoholics who continued drinking showed increased body sway with eyes closed. More recently, investigators have assessed improvement in gait and standing balance with the Walk-a-line Ataxia Battery (Fregly et al. 1972) which consists of three parts: two standing balance measures and one walking measure, each of which is performed first with eyes open and then with eyes closed. Sullivan and colleagues (2000b) found improved performance on Fregly Walk on Floor-Eyes Open and a trend toward better performance on Sharpened Romberg-Eyes Closed (i.e., stand heel-to-toe with arms folded) in a sample of 20 abstinent alcoholics two to twelve months after initial testing at one month of sobriety. Similarly, in a sample of ten abstinent alcoholics, Rosenbloom and colleagues (2007) found a trend toward improved performance on Fregly Eyes Closed ataxia measures (collapsed across tasks) at follow-up testing (mean = two years) after initial testing at about four months mean abstinence, as well as significant associations between ataxia measures and fourth ventricular volume (a proxy index of cerebellar volume) changes. In contrast, Rosenbloom and colleagues (2004) found persistent disturbed eyes closed-one foot

standing balance in 13 alcoholic women (initially tested at 15 weeks abstinence) who had maintained sobriety for 30 to 53 months, suggesting that impairment of this function may be especially resistant to recovery, at least in women.

Although the above longitudinal studies provide evidence for limited partial recovery of gait and balance functions with abstinence, their power and generalizability are limited by small sample sizes. Moreover, conclusions about potential recovery with abstinence have been based on samples with limited abstinence durations. An important question concerns the degree to which recovery may be achieved with more extended abstinence. An additional question regards potential differences between men and women in the severity of alcohol-induced ataxia and in the recovery of gait and balance function with long-term abstinence. Some research suggests that, as a group, women metabolize alcohol differently than men (Li et al. 2000, Lieber 2000), and are more likely than men to experience problems associated with the same level of alcohol consumption (Ely et al. 1999). However, Sullivan and colleagues (2002) reported more mildly impaired gait and balance in a sample of abstinent alcoholic women than was reported for a sample of abstinent men from an earlier study (Sullivan et al. 2000a). In the present study, we employed a large sample (for clinical studies) cross-sectional approach to assess recoverability of gait and balance functions in short-term (6 to 15 weeks) abstinent (STAA; n = 70) and long-term (minimum 18 months, mean = 7.38 years) abstinent (LTAA; n = 82) alcoholics. In addition to comparing abstinence durations, we examined effects of gender and alcohol use variables on Fregly (1972) gait and balance performance.

Methods

Participants

Participants consisted of Non-Alcoholic Controls (NAC, 20 men and 32 women), LTAA (48 men and 34 women) with abstinence durations ranging between 1.5 and 22.38 years (mean = 7.38, SD = 6.26), and STAA (49 men and 21 women), abstinent 6 to 15 weeks. Tables 1 and 2 report demographic information for LTAA and NAC, and STAA and NAC, respectively, along with age-adjusted (based on NAC) Fregly performance measures. Participants were recruited from the community through postings at university campuses, bustops, bulletin boards, stores, laundromats, community centers and health centers. Craig's list, and, referrals from other participants. Alcoholic participants were also recruited from Alcoholics Anonymous (AA), substance abuse treatment centers, and clean and sober transitional houses. All alcoholic participants had attended AA sessions and/or alcohol and drug treatment programs.

Inclusion criteria for the LTAA group were: 1) met lifetime DSM-IV-R (American Psychiatric Association 2000) criteria for alcohol dependence, and 2) were abstinent from alcohol and other drug use (other than nicotine or caffeine) for at least 18 months. For STAA inclusion criteria were 1) met lifetime DSM-IV-R (American Psychiatric Association 2000) and current (within past 12 months) criteria for alcohol dependence, and 2) abstinence from alcohol use for a minimum 6 weeks and maximum 15 weeks, and abstinence from other drug use (other than nicotine or caffeine) for at least 6 weeks. Within LTAA and STAA, participants with a lifetime drug use disorder (DUDL; proportions for each group are reported in Tables 1 – 3) met lifetime DSM-IV-R (American Psychiatric Association 2000) criteria for a drug use disorder. Inclusion criterion for the NAC group were a lifetime drinking average of less than 30 standard

drinks per month, with no periods of drinking more than 60 drinks per month, and no lifetime history of alcohol and substance abuse or dependence (other than nicotine or caffeine).

Exclusion criteria for all three groups were: 1) lifetime or current diagnosis of schizophrenia or schizophreniform disorder using the computerized Diagnostic Interview Schedule (c-DIS) (Bucholz et al. 1991, Erdman et al. 1992, Levitan et al. 1991, Robins et al. 1998), 2) significant history of head trauma or cranial surgery, 4) history of significant neurological disease, 5) history of diabetes, stroke, or hypertension that required an emergent medical intervention, 6) laboratory evidence of hepatic disease, 7) clinical evidence of Wernicke-Korsakoff syndrome, or 8) clinical evidence of a physical condition (e.g., hip, knee, ankle, foot, and/or back injuries; found in 5 STAA and 4 LTAA) that would prevent meaningful interpretation of Fregly (1972) gait and balance measures.

Procedures

Participant screening was initially conducted by a phone interview assessing alcohol use/dependence, use/dependence of other drugs, medical history, and mental health history. All participants were fully informed of the study's procedures and aims, and signed a consent form prior to their participation. Participants completed four sessions that each lasted between an hour and a half and four hours and included clinical, psychiatric, neuropsychological, electrophysiological, and neuroimaging assessments. A trained research associate administered these assessments to all participants. All participants completed all sessions. Non-alcoholic controls were asked to abstain from consuming alcohol for at least 24 hours prior to any lab visit. A Breathalyzer (Intoximeters, Inc., St. Louis, MO) test was administered to all participants. A 0.000 alcohol concentration was required of all participants in

all sessions. A Rapid Screen Test (Oral Fluid Drug Screen) was administered to all participants. A negative result was required of all participants in all sessions. Participants were compensated for their time and travel expenses upon completion of each session. Participants who completed the entire study were also given a completion bonus.

All participants completed the following general assessments: 1) Participants were interviewed on their lifetime drug and alcohol use using the timeline follow-back methodology (Skinner and Allen 1982, Skinner and Sheu 1982, Sobell and Sobell 1990, Sobell et al. 1988), yielding five alcohol consumption measures: Alcohol Peak Dosage, Alcohol Peak Duration, Alcohol Peak Use (Peak Dosage x lifetime days of Peak Use), Alcohol Lifetime Dosage and Alcohol Lifetime Use, 2) medical histories were reviewed in an interview by a trained research associate, 3) blood was drawn to test liver functions, and 4) the Family Drinking Questionnaire was administered based on the methodology of Mann and colleagues (1985) and Stoltenberg and colleagues (1998). The Family Drinking Questionnaire asked participants to rate the members of their family as being alcohol abstainers, alcohol users with no problem, or problem drinkers. Family History Density (FHD) was defined as the proportion of 1st degree relatives that were problem drinkers. 5) psychiatric diagnoses and symptom counts were gathered using the c-DIS (Robins et al. 1998), and additional psychiatric measures included the Reiss-Epstein Anxiety Sensitivity Index (ASI) (Reiss et al. 1986) the State and Trait Scales of the State-Trait Anxiety Inventory for Adults (STAI-S and STAI-T) (Spielberger 1983), the Depression and Hypomania Scales of the Minnesota Multiphasic Personality Inventory-2 (MMPI-D and MMPI-H) (Hathaway and McKinley 1989) the SCID-II (for Borderline Diagnosis), the WISPI IV (Wisconsin Personality Disorder Inventory), and the Socialization Scale of the California Psychological Inventory (CPI-SS) (Gough 1969), and the Psychopathic Deviance Scale of the

MMPI-2 (MMPI-PD) (Hathaway and McKinley 1989). 6) A comprehensive neuropsychological assessment was conducted using the CANTAB (Cambridge Cognition Ltd 2006) battery, supplemented by a number of individual tests with demonstrated sensitivity to damage in brain regions frequently compromised by chronic alcoholism.

Gait and Balance

Gait and standing balance were assessed with the Walk-a-line Ataxia Battery (Fregly et al. 1972) which consisted of three parts, each of which was performed first with eyes open and then with eyes closed: 1) Sharpened Romberg--participants stood with feet placed heel-to-toe, with arms folded across the chest, for a maximum of 60 seconds; 2) Stand on One Leg—each leg was tested separately with a maximum score per trial per foot of 30 seconds; and 3) Walk Heel-to-Toe—the participant walked in a straight line heel-to-toe with arms folded across the chest for a maximum of 10 steps. Each condition was repeated twice, unless a perfect score was obtained on the first trial, in which case the participant received a perfect score. For example, for Stand on Left Leg-Eyes Open, if the participant moved the standing foot, the clock was stopped immediately and the number of seconds stood prior to the violation constituted the trial score. A perfect score on the first trial was weighted two and a perfect score of 60 (30 x 2) was assigned. If the subject required a second trial, the total number of seconds stood on the two trials became the assigned score.

Statistical Analyses

Because the Fregly scores were, for the most part, highly non-parametric, with most participants performing well, and a portion performing poorly, nonparametric (Kruskal-Wallis)

one-way independent groups analyses of variance (ANOVA) examined effects of Group (LTAA vs. NAC, STAA vs. NAC, and LTAA vs. STAA) and (within each group) Gender on the eight Fregly gait and balance performance measures. Because of strong associations of Age with gait and balance measures (assessed with Spearman's r_s), these analyses were conducted with age-adjusted Fregly scores (based on regression in our NAC) as dependent variables. Finally, separate correlational analyses for LTAA and STAA examined associations between Fregly raw scores and alcohol use variables.

Results

LTAA vs. NAC

Table 1 shows male and female LTAA and NAC demographics and mean age-adjusted (based on NAC) scores on Fregly gait and balance measures. Parametric analysis of variance (ANOVA) yielded no significant differences in age between groups (LTAA vs. NAC) or genders, a significant ($p < .001$) Group effect on Years of Education, reflecting more education in NAC than in LTAA, and significant Group ($p < .001$) and Gender ($p = .003$) effects on Family Drinking Density (FDD), reflecting greater proportions of 1st degree relative problem drinkers in LTAA and in women. A chi-square test for independence revealed that the proportion of subjects with a lifetime drug use disorder (DUDL) was not dependent on Gender within LTAA ($\chi^2(1, n = 82) = .116, p = .734$). An odds ratio of 1.17 indicates that LTAA women were about 1.17 times as likely as LTAA men to have a DUDL.

For NAC and LTAA together, Spearman's r_s (one-tailed) yielded significant negative correlations between Age and performance on seven of the eight Fregly measures: Sharpened

Romberg-Eyes Open ($r_s = -.199$, $p = .011$), Stand on Left Leg-Eyes Open ($r_s = -.199$, $p = .011$), Stand on Left Leg-Eyes Closed ($r_s = -.373$, $p < .001$), Stand on Right Leg-Eyes Open ($r_s = -.254$, $p = .002$), Stand on Right Leg-Eyes Closed ($r_s = -.343$, $p < .001$), Walk on floor-Eyes Open ($r_s = -.169$, $p = .025$), and Walk on floor-Eyes Closed ($r_s = -.214$, $p = .006$), all reflecting lower mean scores for older subjects. ANOVA showed no Group by Age interactions.

Nonparametric ANOVA on age-adjusted Fregly scores (See Table 1) yielded a significant Group (LTAA vs. NAC) effect, reflecting poorer performance of LTAA, compared to NAC, on Stand on Right Leg-Eyes Closed ($p = .005$), with trends toward worse performance of LTAA on Sharpened Romberg-Eyes Closed ($p = .099$), Stand on Left Leg-Eyes Closed ($p = .09$), Stand on Right Leg-Eyes Open ($p = .053$), and Walk on Floor-Eyes Closed ($p = .084$).

Nonparametric ANOVA revealed no significant effects of Gender on age-adjusted Fregly scores in either NAC or LTAA. An additional analysis excluded LTAA with a DUDL. LTAA with no DUDL ($n = 38$) still showed impaired performance, relative to NAC, on Eyes-Closed Fregly measures: Sharpened Romberg-Eyes Closed ($p = .015$), Stand on Right Leg-Eyes Closed ($p = .024$), and Walk on Floor-Eyes Closed ($p = .004$).

[Insert Table 1 about here]

STAA vs. NAC

Table 2 shows male and female STAA and NAC demographics and age-adjusted (based on NAC) mean scores on Fregly gait and balance measures. Parametric ANOVA yielded no significant differences in age between groups (STAA vs. NAC) or genders, a significant ($p <$

.001) Group effect on Years of Education, reflecting more education in NAC than in STAA, and a significant Group ($p = .01$) effect on Family Drinking Density (FDD), reflecting greater proportions of 1st degree relative problem drinkers in STAA. A chi-square test for independence (See Table 3) revealed that the proportion of subjects with a lifetime drug use disorder (DUDL) was not dependent on Gender within STAA ($\chi^2 (1, n = 70) = .347, p = .556$). An odds ratio of 1.38 indicates that, within STAA, women were about 1.38 times as likely as men to have a DUDL.

For NAC and STAA together, Spearman's r_s (one-tailed) yielded significant negative correlations between Age and performance on two of the eight Fregly measures: Stand on Left Leg-Eyes Closed ($r_s = -.356, p < .001$), and Stand on Right Leg-Eyes Closed ($r_s = -.225, p < .001$), reflecting lower mean scores for older subjects. ANOVA showed no Group by Age interactions.

Nonparametric ANOVA (See Table 2), with age-adjusted Fregly scores as dependent variables, yielded significant Group (STAA vs. NAC) effects, reflecting poorer performance of STAA, compared to NAC, on Sharpened Romberg-Eyes Open ($p = .031$), Stand on Left Leg-Eyes Open ($p = .047$), Stand on Left Leg-Eyes Closed ($p < .0005$), Stand on Right Leg-Eyes Open ($p = .002$), Stand on Right Leg-Eyes Closed ($p < .0005$), and Walk on Floor-Eyes Closed ($p = .016$). In addition, within all STAA, nonparametric ANOVA revealed significant effects of Gender on age-adjusted Sharpened Romberg-Eyes Closed ($p = .001$) and Stand on Left Leg-Eyes Closed ($p = .049$), reflecting worse performance by STAA women compared to STAA men. Within NAC there were no significant Gender effects. An additional analysis excluded STAA with a DUDL. Although the smaller sample provided less power, STAA with no DUDL ($n = 27$) still showed impaired performance, relative to NAC, on Stand on Left Leg-Eyes Closed ($p =$

.012), Stand on Right Leg-Eyes Open ($p = .048$), Stand on Right Leg-Eyes Closed ($p = .018$), and Walk on Floor-Eyes Closed ($p = .016$).

[Insert Table 2 about here]

STAA vs. LTAA

Table 3 shows demographics, mean Abstinence Durations, Lifetime Alcohol Use means, and mean age-adjusted Fregly scores for LTAA and STAA men and women. Parametric ANOVA showed that LTAA were significantly ($p = .01$) older than STAA, there were no main or interactive effects on Years of Education, and women had a significantly ($p = .015$) higher proportion of first degree relative problem drinkers than men. In addition, LTAA had significantly ($p < .001$) longer Abstinence Duration than STAA, and men had significantly ($p = .013$) greater Lifetime Alcohol Use than women. Finally, chi-square tests for independence revealed that the proportion of subjects with a lifetime drug use disorder (DUDL) was not dependent on Group ($\chi^2(1, n = 152) = .931, p = .334$), Gender within STAA ($\chi^2(1, n = 70) = .347, p = .556$), or Gender within LTAA ($\chi^2(1, n = 82) = .116, p = .734$). An odds ratio of 1.37 indicates that STAA were about 1.37 times as likely as LTAA to have a DUDL.

For STAA and LTAA together, Spearman's r_s (one-tailed) yielded significant negative correlations between Age and performance on five of the eight Fregly measures: Stand on Left Leg-Eyes Open ($r_s = -.160, p = .025$), Stand on Left Leg-Eyes Closed ($r_s = -.323, p < .001$), Stand on Right Leg-Eyes Open ($r_s = -.223, p = .003$), Stand on Right Leg-Eyes Closed ($r_s = -.219, p = .003$), and Walk on floor-Eyes Closed ($r_s = -.219, p = .003$), all reflecting lower mean

scores for older subjects. ANOVA showed no Group by Age interactions.

Nonparametric ANOVA assessing effects of Group (LTAA vs. STAA) on age-adjusted Fregly performance (See Table 3) yielded significant Group (STAA vs. LTAA) effects, reflecting overall better performance of LTAA, compared to STAA, on Sharpened Romberg-Eyes Open ($p = .012$), Stand on Left Leg-Eyes Closed ($p = .015$), and Stand on Right Leg-Eyes Closed ($p = .040$). In addition, within STAA (but not LTAA) nonparametric ANOVA (using Fregly age-adjusted scores) revealed significant effects of Gender on Sharpened Romberg-Eyes Closed ($p = .003$) and Stand on Left Leg-Eyes Closed ($p = .049$), reflecting worse performance by STAA women than STAA men.

[Insert Table 3 about here]

Correlations of Alcohol Use Measures with Fregly Measures in STAA and LTAA

In STAA, of the alcohol use measures described in our Methods, Alcohol Lifetime Dose (standard drinks) was significantly negatively correlated with Sharpened Romberg-Eyes Closed ($r_s = -.291$, $p = .049$), Stand on Left Leg-Eyes Closed ($r_s = -.328$, $p = .026$), and Walk on Floor-Eyes Open ($r_s = -.295$, $p = .047$), and there were trends toward negative associations between Alcohol Lifetime Dose and Stand on Left Leg- Eyes Open ($r_s = -.249$, $p = .095$), and Walk on Floor-Eyes Closed ($r_s = -.259$, $p = .083$). In addition, Alcohol Peak Dose (standard drinks) was negatively correlated with Sharpened Romberg-Eyes Closed ($r_s = -.238$, $p = .048$), Stand on Left Leg- Eyes Closed ($r_s = -.244$, $p = .042$), and there was a trend toward a negative association between Alcohol Peak Dose and Stand on Right Leg-Eyes Closed ($r_s = -.215$, $p = .073$). Finally,

after partialing out Age, there was a trend ($r_s = -.237$, $p > .05$) toward a negative association between Alcohol Lifetime Use (standard drinks) and Stand on Left Leg-Eyes Closed.

In LTAA, only Alcohol Lifetime Use Duration and Alcohol Lifetime Use were correlated with Fregly gait and balance scores in LTAA. After partialing out Age, Alcohol Lifetime Use Duration significantly negatively correlated with performance on Sharpened Romberg-Eyes Closed ($r_s = -.229$, $p = .04$), Stand on Left Leg, Eyes Open, ($r_s = -.314$, $p = .004$), Stand on Right Leg-Eyes Open ($r_s = -.405$, $p < .001$) and Stand on Right Leg-Eyes Closed ($r_s = -.227$, $p = .042$). In addition, Alcohol Lifetime Use was negatively associated with Stand on Right Leg-Eyes Open performance ($r_s = -.242$, $p = .03$). Length of Abstinence was not significantly associated with any of the Fregly measures for either STAA or LTAA.

Discussion

The central findings of the current study were 1) disturbed gait and balance in STAA, and disturbed standing balance in LTAA, 2) overall less impaired gait and balance in LTAA, compared to STAA, and 3) worse performance of STAA (but not LTAA) women, compared to men, on two standing balance measures. These results, discussed separately below, have implications regarding patterns of alcohol related impairment, and potential recovery with sustained abstinence, of gait and balance abilities.

First, our results are consistent with previous findings (Gilman et al. 1990, Rosenbloom et al. 2004, 2007, Sullivan et al. 2000a, 2000b, 2000c) that impaired gait and balance are among the most salient deficits found in active and recently detoxified alcoholics. Moreover, significantly impaired performance of our LTAA on one eyes-closed standing balance measure,

with trends toward impaired performance on four other Fregly measures, indicates that deficits persist, even with extended (mean = 7.38 years) abstinence. Impaired eyes-closed performance was not due to a relatively large proportion of LTAA with a DUDL. The persistent impaired performance of LTAA on Right Leg-Eyes-closed standing balance is consistent with results from a longitudinal study by Rosenbloom and colleagues (2004), who found disturbed eyes-closed standing balance in 13 alcoholic women (initially tested at 15 weeks abstinence) who had maintained sobriety for 30 to 53 months. Given the considerably more extended abstinence durations of our LTAA, our results provide evidence that disturbed performance on standing balance measures, especially with eyes closed, may be particularly resistant to recovery. Moreover, a lack of gender differences in our LTAA in performance on any of the gait and balance measures reflects similar profiles of persistent impairment for LTAA men and women.

Second, in contrast with LTAA, who were significantly impaired, relative to NAC, on only one Fregly measure, STAA were significantly impaired on six Fregly measures, including five eyes-open and eyes-closed standing balance measures and an eyes-closed walking measure. Moreover, LTAA performed significantly better than STAA on Sharpened Romberg-Eyes Closed, Stand on Left Leg-Eyes Closed, and Stand on Right Leg-Eyes Closed. The differences we found between STAA and LTAA in gait and balance performance could be due to group differences not associated with abstinence duration. That is, alcoholics who are likely to achieve long-term abstinence may represent a population that is less susceptible than STAA to disturbances of gait and balance. However, our STAA and LTAA did not differ with respect to lifetime alcohol consumption (Alcohol Lifetime Use), family drinking density (proportion of first degree relative problem drinkers), years of education, or proportion of individuals with a lifetime drug use disorder (DUDL). Rather, although our design was cross-sectional, our results are

consistent with evidence from longitudinal studies (Diener et al. 1984, Rosenbloom et al. 2007, Sullivan et al. 2000b) for partial recovery of gait and balance performance with sustained abstinence from alcohol. Results from our study, with a considerably larger ($n = 82$) LTAA sample and longer mean abstinence durations extend these findings, providing evidence suggesting that continuing recovery from ataxia, particularly with visual control, may be achieved with more extended sobriety. While STAA were significantly impaired, relative to NAC, on standing balance measures both with and without visual control, LTAA were significantly impaired only on standing balance without visual control. This is consistent with earlier findings (Diener et al. 1984, Scholz et al. 1986) that body sway, associated with anterior cerebellar atrophy, may be partially compensated by visual control. In fact, in general, given that standing balance with visual control is easier than without, recovery from alcohol-induced damage that can lead to ataxia (e.g., cerebellar atrophy, peripheral neuropathy, dopaminergic denervation), is likely to be seen first in those balance measures performed with eyes open.

A third finding of the present study was that, in STAA, women performed worse than men on two static balance measures (Romberg-Eyes Closed, and Stand on Left Leg-Eyes Closed). Given that in NAC and LTAA we found no Gender differences in performance on Fregly measures, these findings suggest that alcohol dependence may result in more severe gait and balance disturbances for women than for men, but that with very long-term abstinence, women display a pattern of partial recovery and limited persistent impairment that is comparable to men. It should be noted that a somewhat higher proportion of DUDL in STAA women than men could contribute to the more severe deficits on the two standing balance measures. However, as reported above, a chi-square test of independence showed that the proportion of DUDL in STAA was not dependent on gender.

The finding of more severely disturbed eyes-closed standing balance in our STAA women than in our STAA men is consistent with evidence that, as a group, women metabolize alcohol differently than men (Li et al. 2000, Lieber 2000) and are more likely than men to experience problems associated with the same level of alcohol consumption (Ely et al. 1999). Indeed, our STAA women had significantly lower lifetime alcohol burden (alcohol lifetime use) than our STAA men. Alternatively, the more severely impaired performance of our STAA women could be a function a higher threshold for women in alcohol-related problems before receiving treatment (Dawson 1996, Schober and Annis 1996), leading to an over-representation of the most severely affected women in treatment samples. However, this explanation seems less viable in light of the significantly lower lifetime alcohol consumption in our STAA women, compared to men. The finding of more severe deficits in STAA women on the two measures of standing balance without visual control appears at be at odds with the results of Sullivan and colleagues (2002), who reported more mildly impaired gait and balance function in a sample of abstinent alcoholic women than for a sample of abstinent men from an earlier study (Sullivan et al. 2000a). However, the discrepancy could be due to a difference (albeit, relatively small) in abstinence durations between the women in Sullivan and colleagues' (2002) study, who had been abstinent for an average 3.6 months, compared to one month abstinence in men from the earlier Sullivan and colleagues' (2000a) study.

In conclusion, our results extend findings of smaller sample longitudinal studies, providing evidence that alcoholics continue to recover from ataxia (especially with visual control) with long-term abstinence. However, even extended abstinence may not be sufficient for recovery of standing balance without visual control. Recognizing the limitations of cross-

sectional studies, future investigations may employ large sample longitudinal designs to explore effects of extended abstinence on alcoholics' prospects for recovery from ataxia.

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Table 1. Male and Female LTAA and NAC demographics and mean scores on Fregly gait and balance measures. Effect sizes for demographic variables are reported from parametric ANOVA. P levels for Group and Gender effects on Fregly performance are reported from nonparametric ANOVA conducted with age-adjusted (based on NAC) Fregly scores as dependent variables. Correlations between Age and Fregly measures (across Group) are reported from Spearman's r_s .

Variables	Long-Term Abstinent		Non-Alcoholic Controls		% Variance Accounted For (η^2)			
	Men (n=48)	Women (n=34)	Men (n=20)	Women (n=32)	Group	Gender	Group x Gender	
Demographics								
Age (years)	49.00 ± 6.88	47.58 ± 5.85	46.70 ± 7.00	48.41 ± 7.66	0.3	0.0	1.2	
Years Education	13.60 ± 2.54	13.43 ± 2.34	15.65 ± 2.58	16.00 ± 2.48	16.9**	0.0	0.3	
Proportion 1 st Degree Relative Problem Drinkers ^a	0.25 ± 0.29	0.44 ± 0.30	0.10 ± 0.15	0.20 ± 0.22	12.1**	7.1**	0.9	
Proportion with a Lifetime Drug Use Disorder ^b	.52	.56	n/a	n/a	n/a	n/a	n/a	
Fregly Gait and Balance Measures					Age (r_s)	Group (p)	LTAA Gender (p)	NAC Gender (p)
Romberg, Eyes Open	117.66 ± 16.43	115.31 ± 13.50	119.80 ± 1.48	116.91 ± 12.63	-.199*	.965	.118	.792
Romberg, Eyes Closed	67.29 ± 47.15	69.21 ± 45.55	76.79 ± 43.91	88.98 ± 40.57	-.060	.099	.825	.516
Stand on Left Leg, Eyes Open	50.15 ± 17.47	53.41 ± 15.16	57.73 ± 6.80	53.80 ± 14.85	-.199*	.523	.689	.424
Stand on Left Leg, Eyes Closed	16.99 ± 15.64	17.18 ± 14.08	22.90 ± 16.88	21.60 ± 15.51	-.373**	.090	.981	.665
Stand on Right Leg, Eyes Open	48.35 ± 19.02	51.70 ± 15.27	56.32 ± 11.64	56.11 ± 12.39	-.254**	.053	.992	.714
Stand on Right Leg, Eyes Closed	13.59 ± 10.91	15.67 ± 12.25	25.02 ± 18.29	21.67 ± 15.94	-.343**	.005**	.495	.658
Walk Floor, Eyes Open	18.95 ± 3.33	18.23 ± 4.38	19.97 ± 0.20	19.14 ± 3.02	-.169*	.585	.316	.962
Walk Floor, Eyes Closed	12.94 ± 6.44	12.49 ± 6.04	12.72 ± 6.16	15.41 ± 6.12	-.214**	.084	.516	.100

Measures are reported mean ± standard deviation. Effect is significant: * $p \leq 0.05$, ** $p \leq 0.01$.

^a: n = 46 for LTAA Men, n = 33 for LTAA Women, n = 30 for NAC Women.

^b: % variance accounted for (η^2) cannot be computed for Proportion with a Lifetime Drug use Disorder (a nominal variable). Odds ratios are reported in the text of our results.

Table 2. Male and Female STAA and NAC demographics and mean scores on Fregly gait and balance measures. Effect sizes for demographic variables are reported from parametric ANOVA. P levels for Group and Gender effects on Fregly performance are reported from nonparametric ANOVA conducted with age-adjusted (based on NAC) Fregly scores as dependent variables. Correlations between Age and Fregly measures (across Group) are reported from Spearman's r_s .

Variables	Short-Term Abstinent		Non-Alcoholic Controls		% Variance Accounted For (η^2)			
	Men (n=49)	Women (n=21)	Men (n=20)	Women (n=32)	Group	Gender	Group x Gender	
Demographics								
Age (years)	44.85 ± 7.08	45.74 ± 6.41	46.70 ± 7.00	48.41 ± 7.66	2.2	0.7	0.1	
Years Education	13.26 ± 1.88	13.62 ± 1.88	15.65 ± 2.58	16.00 ± 2.48	21.5**	0.6	0.0	
Proportion 1 st Degree Relative Problem Drinkers ^a	0.25 ± 0.29	0.30 ± 0.30	0.10 ± 0.15	0.20 ± 0.22	5.6*	2.0	0.2	
Proportion with a Lifetime Drug Use Disorder ^b	.59	.67	n/a	n/a	n/a	n/a	n/a	
Fregly Gait and Balance Measures					Age (r_s)	Group (p)	STAA Gender (p)	NAC Gender (p)
Romberg, Eyes Open	119.06 ± 2.57	101.64 ± 31.62	119.80 ± 1.48	116.91 ± 12.63	-.011	.031*	.321	.792
Romberg, Eyes Closed	83.41 ± 46.28	47.29 ± 43.94	76.79 ± 43.91	88.98 ± 40.57	-.002	.596	.003**	.516
Stand on Left Leg, Eyes Open	52.48 ± 13.09	47.40 ± 21.21	57.73 ± 6.80	53.80 ± 14.85	-.130	.047*	.974	.424
Stand on Left Leg, Eyes Closed	14.99 ± 15.93	6.75 ± 8.51	22.90 ± 16.88	21.60 ± 15.51	-.356**	< .0005**	.049*	.665
Stand on Right Leg, Eyes Open	50.56 ± 16.95	48.38 ± 19.08	56.32 ± 11.64	56.11 ± 12.39	-.095	.002**	.969	.714
Stand on Right Leg, Eyes Closed	11.97 ± 12.13	9.58 ± 9.64	25.02 ± 18.29	21.67 ± 15.94	-.225**	< .0005**	.469	.658
Walk Floor, Eyes Open	19.71 ± 1.46	18.85 ± 3.02	19.97 ± 0.20	19.14 ± 3.02	.000	.125	.793	.962
Walk Floor, Eyes Closed	12.00 ± 6.41	10.72 ± 6.76	12.72 ± 6.16	15.41 ± 6.12	-.056	.016*	.469	.100

Measures are reported mean ± standard deviation. Effect is significant: * $p \leq 0.05$, ** $p \leq 0.01$.

^a : n = 47 for STAA Men, n = 30 for NAC Women.

^b : % variance accounted for (η^2) cannot be computed for Proportion with a Lifetime Drug Use Disorder (a nominal variable). Odds ratios are reported in the text of our results.

Table 3. Male and Female STAA and LTAA demographics and mean scores on Fregly gait and balance measures. Effect sizes for demographic variables are reported from parametric ANOVA. P levels for Group and Gender effects on Fregly performance are reported from nonparametric ANOVA conducted with age-adjusted (based on NAC) Fregly scores as dependent variables. Correlations between Age and Fregly measures (across Group) are reported from Spearman's r_s ...

Variables	Short-Term Abstinent		Long-Term Abstinent		% Variance Accounted For (η^2)			
	Men (n=49)	Women (n=21)	Men (n=48)	Women (n=34)	Group	Gender	Group x Gender	
Demographics								
Age (years)	44.85 ± 7.08	45.74 ± 6.41	49.00 ± 6.88	47.58 ± 5.85	4.0*	0.0	0.7	
Years Education	13.26 ± 1.88	13.62 ± 1.88	13.60 ± 2.54	13.43 ± 2.34	0.0	0.0	0.3	
Proportion 1 st Degree Relative Problem Drinkers ^a	0.25 ± 0.29	0.30 ± 0.30	0.25 ± 0.29	0.44 ± 0.30	1.2	4.1*	1.4	
Abstinence Duration (years)	70.24 ± 21.52	69.30 ± 24.76	2471.77 ± 2151.78	3001.76 ± 2343.31	37.1**	0.6	0.6	
Alcohol Lifetime Use	75830.87 ± 68561.39	46833.77 ± 39212.71	70463.13 ± 61541.89	47289.92 ± 57076.42	0.0	4.1*	0.1	
Proportion with a Lifetime Drug Use Disorder (p is reported for Chi ²)	.59	.67	.52	.56	Group p > .33	STAA Gender p > .55	LTAA Gender p > .73	
Fregly Gait and Balance Measures					Age (r_s)	Group (p)	STAA Gender (p)	LTAA Gender (p)
Romberg, Eyes Open	119.06 ± 2.57	101.64 ± 31.62	117.66 ± 16.43	115.31 ± 13.50	-.070	.012*	.321	.118
Romberg, Eyes Closed	83.41 ± 46.28	47.29 ± 43.94	67.29 ± 47.15	69.21 ± 45.55	-.078	.336	.003**	.825
Stand on Left Leg, Eyes Open	52.48 ± 13.09	47.40 ± 21.21	50.15 ± 17.47	53.41 ± 15.16	-.160*	.158	.974	.689
Stand on Left Leg, Eyes Closed	14.99 ± 15.93	6.75 ± 8.51	16.99 ± 15.64	17.18 ± 14.08	-.323**	.015*	.049*	.981
Stand on Right Leg, Eyes Open	50.56 ± 16.95	48.38 ± 19.08	48.35 ± 19.02	51.70 ± 15.27	-.223**	.241	.969	.992
Stand on Right Leg, Eyes Closed	11.97 ± 12.13	9.58 ± 9.64	13.59 ± 10.91	15.67 ± 12.25	-.219**	.040*	.469	.495
Walk Floor, Eyes Open	19.71 ± 1.46	18.85 ± 3.02	18.95 ± 3.33	18.23 ± 4.38	-.124	.254	.793	.316
Walk Floor, Eyes Closed	12.00 ± 6.41	10.72 ± 6.76	12.94 ± 6.44	12.49 ± 6.04	-.219**	.337	.469	.516

Measures are reported mean ± standard deviation. Effect is significant: * $p \leq 0.05$, ** $p \leq 0.01$.

^a : n = 47 for STAA Men, n = 33, n = 46 for LTAA men, n = 33 for LTAA women.