Effect of Vision, Touch and Stance on Cerebellar Vermian-related Sway and Tremor: A Quantitative Physiological and MRI Study

Postural balance is impaired in individuals with pathology of the anterior superior vermis of the cerebellum. Chronic alcoholism, with its known vermian pathology, provides a viable model for studying the relationship between cerebellar pathology and postural stability. Decades of separate study of recovering alcoholics and post-mortem neuroanatomical analysis have demonstrated vermian pathology but few studies have used quantitative posturography, acquired concurrently with quantitative neuroimaging, to establish whether this brain-structure-function relationship is selective in vivo. Here, 30 healthy men and 39 chronic alcoholic men, abstinent from alcohol for several months, underwent MRI for volumetric quantitation of the cerebellar vermis and three comparison brain regions, the cerebellar hemispheres, supratentorial cortex and corpus callosum. All subjects also participated in an experiment involving a force platform that measured sway path length and tremor during static standing balance under four sensory conditions and two stance conditions. Three novel findings emerged: (i) sway path length, a physiological index of postural control, was selectively related to volume of the cerebellar vermis and not to any comparison brain region in the alcoholics; (ii) spectral analysis revealed sway prominence in the 2–5 Hz band, another physiological sign of vermian lesions and also selectively related to vermian volume in the alcoholics; and (iii) despite substantial postural sway in the patients, they successfully used vision, touch and stance to normalize sway and reduce tremor. The selective relationship of sway path to vermian but not lateral cerebellar volume provides correlational evidence for functional differentiation of these cerebellar regions. Improvement to virtual normal levels in balance and reduction in sway and tremor with changes in vision, touch and stance provide evidence that adaptive mechanisms recruiting sensorimotor integration can be invoked to compensate for underlying cerebellar vermian-related dysfunction.

Keywords: alcoholism, cerebellum, MRI, postural control, posturography, tremor, vermis

Introduction

Postural balance is impaired in individuals with pathology of the anterior superior vermis of the cerebellum. Patients commonly targeted for such study have been detoxified alcoholics because of their presumed, selective compromise of the anterior lobules of the vermis (Victor et al., 1989). A number of the most cited studies (e.g. Mauritz et al., 1979; Diener et al., 1984; Baloh et al., 1986) examined individuals with a history of alcohol dependence. Although chronic alcoholism can cause significant damage to the anterior vermian lobules, evidenced neuropathologically (Victor et al., 1989; Harper and Kril, 1993; Baker et al., 1999) and neuroradiologically (Gilman et al., 1990; Martin et al., 1995; Sullivan et al., 2000a), focal vermian pathology was only presumed to be present in the patients in the posture and gait studies (e.g. Mauritz et al., 1979; Scholz et al., 1986; Ledin and Odvikst, 1991). Recent support for an anterior vermian substrate of voluntary, upright postural control derives from PET 15O studies of healthy subjects (Ouchi et al., 1999, 2001). Following posturography recorded in five different positions, from supine, to sitting, to standing, subjects with better standing balance control had greater regional blood flow in the anterior superior lobules of the vermis. In vivo MRI verification of the vermian structural underpinnings of alcohol-related compromise of postural control measured with quantitative physiological analysis, however, has not been reported and was a principal aim of the present study.

If a relationship between exaggerated physiological sway and vermian volume shrinkage is present in abstinent alcoholics, the question remains whether excessive sway stemming from such a central nervous system substrate can be ameliorated by sensory or motor information known to reduce sway in healthy individuals without vermian lesions (Jeka and Lackner, 1994), in patients with presumed anterior vermian lesions (Diener and Dichgans, 1992; Roebuck et al., 1998) and in patients with spinocerebellar lesions (Dichgans and Diener, 1989). We devised an experiment to manipulate vision, touch and stance, while acquiring physiological measures of static postural control with a force platform, yielding sway paths and changes in pressure exerted independently in the anterior-posterior and medial-lateral planes relative to the individual (Nashner and Peters, 1990; McCollum et al., 1996). Vision and touch are perceptually-based cues, whereas changes in stance width can exert biomechanical effects on postural stability (Wintner et al., 1998, 2001). Accordingly, data analysis focusing on stance compared with perceptual cues took into account these potential qualitative differences in the type of information imparted under these different conditions. We tested the hypothesis that alcoholics would exhibit excessively long sway paths, notable in the anterior-posterior direction, relative to controls when standing without the benefit of sensory or stance aids, and that introduction of cues would attenuate but not necessarily ameliorate imbalance.

Finally, lesions of the anterior lobes of the vermis characteristically result in postural tremor (~5 Hz) (Gilman et al., 1981; Diener et al., 1984; Neiman et al., 1990), which, like sway, is especially prominent in the anterior-posterior direction (Victor et al., 1959; Mauritz et al., 1979). Here, we performed spectral analysis of sway velocity (Baloh et al., 1998) to test the hypotheses that alcoholics would show increased power in the 2–5 Hz range that would correlate with volume of the
and touch [touch (Tch) or no touch (NoTch)]. These conditions yielded eight combinations: EO-FA-Tch, EO-FA-NoTch, EO-FT-Tch, EO-FT-NoTch, EC-FA-Tch, EC-FA-NoTch, EC-FT-Tch and EC-FT-NoTch. In the touch conditions, subjects placed their right-hand index finger on a device made of a break-away piece of plastic tubing, incapable of bearing body weight and affixed to a vertical pole, also made of plastic tubing and adjustable to the height of a subject. In all non-touch conditions, subjects relaxed both arms and hands at their sides. Subjects stood barefoot in the center of the platform for three 30 s trials for each of the eight conditions, which were balanced across subjects. Figure 1 presents examples of sway paths without any cues and with three cues.

### Materials and Methods

#### Subjects

The alcoholic group comprised 39 men (age 34–75 years), who were recruited from local rehabilitation centers and met DSM-IV criteria for alcohol substance dependence (mean duration of alcoholism = 20 ± 10.3 years). On average (median), these men had refrained from drinking alcohol for 65 days. The control group comprised 30 age-matched men (age 30–73 years), recruited from the local community. All subjects underwent a thorough examination to identify the following exclusionary criteria: presence of DSM-IV (American Psychiatric Association, 1994) Axis I diagnoses of Bipolar Disorder or Schizophrenia, history of alcohol substance dependence, alcohol-related amnestic disorder, CNS trauma (such as loss of consciousness for >50 min, seizures not related to alcohol withdrawal), degenerative disease or serious medical condition (such as insulin-dependent diabetes, signs of hepatic disorder). All subjects were volunteers, gave written informed consent, obtained according to the Declaration of Helsinki and the Ethical Committee of Stanford University School of Medicine and SRI International, to participate in this study and were paid a modest stipend for participation. Prior to testing, all subjects had breath alcohol determination and none was tested if the level exceeded 0.03.

The groups did not differ significantly in age, handedness, body mass index, parental socioeconomic status, or estimated premorbid IQ [National Adult Reading Test (Nelson, 1992)]. Neither did the groups differ significantly in height [t(65) = 1.42, P = 0.1602]; the alcoholic group was 177.9 ± 6.7 cm and the control group was 175.5 ± 6.9 cm. On average, the alcoholes consumed –10 times as much alcohol over their lifetime than the controls [t(65) = 5.822, P = 0.0001]. Table 1 presents demographic data for the two groups.

Most subjects were also interviewed to obtain a history of falls experienced over the past year, regardless of drinking status (Tinetti et al., 1995a,b). Alcoholics reported having experienced more falls over the prior year than controls (χ² = 5.838, P = 0.0157). Whereas 58% (22 of 38) mentioned other alcoholics, only 16% (9 of 55) of controls. These cases were excluded prior to calculation of the demographic descriptives in Table 1.

### MRI Acquisition and Analysis

All alcoholics and controls underwent MRI structural scanning. Prior to quantitative analysis, images were read by a clinical neuroradiologist to identify space occupying lesions or other dysmorphology that would be indicative of neuropathology other than the target conditions or that would interfere with morphometric analysis. Additional review of images identified studies of quality too poor for quantification. One case was excluded for an enlarged blood vessel in the cerebellum, and another was excluded for neuroradiological evidence for liver disease (hypointensities in the basal ganglia suggestive of significant iron deposition). These cases were excluded prior to calculation of the demographic descriptives in Table 1.

#### Infratentorial Regions: Cerebellar Anterior Superior Vermis and Hemispheres

Cerebellar morphometric quantification was based on a semi-automated segmentation using the image intensity histogram of thin-slice, late-echo, fast spin-echo (FSE) images (94 2-mm-thick slices; T₂/T₁ = 11 050/98 ms, matrix = 256 × 192), which were resampled into 1 mm isotropic voxels and provided high fluid-tissue conspicuity. The bimodal intensity distribution was discrete in all cases, and an operator selected the minima between peaks. Prior to analysis, images were realigned first in the axial plane so that the cerebellar-interhemispheric fissure was perpendicular to the bottom of the image frame, and then in the sagittal plane so that the fourth ventricle was perpendicular to the bottom of the image frame (Cournoske et al., 1989, 1994; Deshmukh et al., 1997).

The anterior-superior vermis sample was measured on seven 1-mm-thick, aligned and extracted sagittal slices — the mid-sagittal and three 1-mm-thick parasagittal slices taken from left and right of the midline. The cerebellar hemisphere sample was measured on five 1-mm-thick slices, which were extracted at the widest diameter of a projection image of the entire brain. The tissue margins were manually identified on aligned and extracted coronal images, guided by the landmarks described in the atlas of Schmahmann et al. (2000). All scoring was conducted manually and blind to subject identification.

#### Supratentorial Regions: Cortical Gray Matter and Corpus Callosum

Cortical gray matter volume was derived from an automated segmentation using a spoiled gradient recalled echo MRI data (SPGR, 94 2-mm thick slices; T₂/T₁ = 25/5 ms, flip angle = 30°, matrix = 256 × 192). We used the FSL Brain Extraction Tool (BET) (Smith, 2002) to extract brain from SPGR images and FLS FAST (Zhang et al., 2001; Smith, 2002), a k-means clustering algorithm to identify gray matter, white matter and CSF compartments. For the present analysis, the cortical gray matter volume was defined as all gray matter voxels identified in the outer 45% rim (Pfefferbaum et al., 1994) of all supratentorial slices, i.e. all slices above the anterior commissure/posterior commissure plane and perpendicular to the midline.

### Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Age</th>
<th>Parental socioeconomic status</th>
<th>NART IQ*</th>
<th>Body mass index</th>
<th>Lifetime alcohol consumption (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcoholic (n = 39)</td>
<td>52.4 ± 10.3</td>
<td>34.8 ± 12.6</td>
<td>110.4 ± 8.3</td>
<td>27.4 ± 4.1</td>
<td>1045.1 ± 679.7</td>
</tr>
<tr>
<td>Control (n = 30)</td>
<td>51.9 ± 12.6</td>
<td>38.0 ± 15.7</td>
<td>113.9 ± 6.2</td>
<td>27.3 ± 4.4</td>
<td>727.7 ± 74.4</td>
</tr>
<tr>
<td>t-test P-value</td>
<td>n.s.</td>
<td>n.s.</td>
<td>0.07</td>
<td>n.s.</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

*NART = National Adult Reading Test, an estimate of premorbid intelligence quotient (IQ).
The area of the corpus callosum was identified on the midsagittal slice extracted from the SPGR data with a semi-automated edge identification procedure. Prior to segmentation, the silhouette of the corpus callosum was rotated to a plane parallel to the inferior extremes of the rostrum anteriorly and splenium posteriorly. Following the automated routine, the borders of the corpus callosum were manual edited to remove non-target voxels (Sullivan et al., 2002; Schulte et al., 2003).

An estimate of supratentorial intracranial volume (ICV) was derived using interactive software that allowed the operator to determine dural margins for left, right and superior parietal lobe and inferior temporal lobe using the coronal image; and for anterior frontal and posterior occipital lobes using the sagittal image. The ICV provided the basis for correcting regional brain volumes for normal variation in head size (cf. Mathalon et al., 1993; Pfefferbaum et al., 1994).

Figure 1. Examples of sway paths (anterior-posterior and medial-lateral directional average) for one trial performed by a 61-year-old control (top) and a 59-year-old alcoholic (bottom). The left panel of sway paths displays performance without any experimental cues (EC-FT-NoTch), and the right panel shows performance when provided all three experimental cues (EO-FA-Tch). Note the anterior-posterior sway in the alcoholic’s path even with cues.

Figure 2. Means ± SE sway path lengths for the feet together and feet apart conditions with eyes open versus closed and with and without touch for the two subject groups.
Correction of Regional Brain Volumes for Intracranial Volume and Age

Prior studies have reported age-related decline in cerebellar volume, notable in the vermis (Luft et al., 1999; Sullivan et al., 2000a; Woodruff-Pak et al., 2001; Raz et al., 2003), and also in the comparison brain regions: cerebellar hemispheres (Sullivan et al., 2000a; Raz et al., 2003), cerebral cortex (Pfefferbaum et al., 1994; Raz et al., 1997) and corpus callosum (Salat et al., 1997; Sullivan et al., 2002). Consequently, regional volumes were expressed as standardized Z-scores, adjusted with linear regression for normal variation in intracranial volume of the supratentorium and age (Pfefferbaum et al., 1992, 1994). The control mean ± SD equaled 0 ± 1, and the volumes of the alcoholics were expressed as deviations from the controls.

Statistical Analysis

The sway path data were subjected to repeated-measures analyses of variance (ANOVA). A pair of ANOVAs focused on the effects of vision and touch cues irrespective of stance; accordingly, one ANOVA compared vision and touch cues in the feet apart conditions, and the other ANOVA was based on the feet together conditions. Where appropriate, Geiser-Greenhouse correction was applied.

Correlations between sway path lengths and alcoholism factors or regional brain volumes were tested with Pearson correlations. Multiple regression analysis was used to test for specificity of brain structure-function relationships.

We also performed separate frequency analyses (fast Fourier transform) on the anterior-posterior and lateral-medial sway path velocity (the two-point differential of the filtered sway path). Following the method of Baloh and colleagues (Baloh et al., 1994, 1998) to characterize the frequency (Hz) of maximal sway velocity, we derived a frequency quotient, which was the power of the spectral frequencies between 2 and 5 Hz divided by those between 0 and <2 Hz, with the expectation that the alcoholics would have a higher ratio than controls. Because prior work had shown that frequency analysis of center of pressure sway path velocity (distance/time) to be more sensitive than amplitude (distance) (Baloh et al., 1998), only velocity was subjected to frequency analysis.

Results

Sway Path Length and Direction: Effect of Vision, Touch and Stance

Vision and Touch Cues Irrespective of Stance Differences

Separate repeated-measures ANOVAs (two group × two touch conditions × two vision conditions) compared performance with and without visual and touch cues irrespective of stance: one ANOVA was based on scores from the feet together conditions and the other with feet apart (Fig. 2). These two ANOVAs yielded a similar pattern of group × cue type interactions, where alcoholics showed greater sway path reduction than controls with vision than touch cues that was significant with feet together [F(1,67) = 7.865, P = 0.0066] and showed a trend with feet apart [F(1,67) = 3.163, P = 0.0799]. The three-way interaction of group-by-cue type-by-cue presence was significant with feet together [F(1,67) = 9.924, P = 0.0024] but not with feet apart [F(1,67) = 0.619, P = 0.43]. Comparable analyses based on the root mean square of the sway path were insensitive to group differences or group × cue condition interactions observed with sway path length.

Stance Differences and Sway Direction Irrespective of Vision or Touch Cues

Potential group differences in preferential sway direction (that is, anterior-posterior versus medial-lateral) were examined by comparing the mean sway path length of the feet together versus feet apart conditions, regardless of presence of visual or tactual cues. A repeated-measures ANOVA for group, condition, and direction yielded two interactions involving group: one with direction [F(1,67) = 10.428, P = 0.0019] and a trend with condition [F(1,67) = 2.736, P = 0.1028]. Thus, compared with controls, alcoholics exhibited relatively more sway in the anterior-posterior direction irrespective of condition.

Effect of Practice and Fatigue

Each path length was calculated as the mean of three trials per condition. To test for differential learning or fatigue across trials, interactions from two group × three trial ANOVAs were sought for each set of cue conditions. Without cues, the alcoholics tended to show greater improvement than controls [F(2,134) = 2.883, P < 0.06] over the three trials but, as noted above, never achieved control performance levels. The same pattern was observed for the eyes-open single-cue condition [group × trial interaction, F(2,134) = 3.674, P = 0.028] but not for any pair of cues or all three cues. Thus, there was no evidence of fatigue-induced exacerbation of sway over the three 30 s trials and a suggestion of improvement over trials.

Frequency Analysis of Sway Velocity

A frequency analysis focused on differences in the direction of sway in the vision and stance conditions between the two groups (Fig. 3). The power of the sway velocity spectrum was expressed as a frequency quotient (2–5 Hz/0–2 Hz). Repeated measures ANOVAs revealed group-by-direction interactions, with eyes closed [feet together, F(1,67) = 4.886, P = 0.0305; feet apart, F(1,67) = 3.193, P = 0.0785] and with eyes open and feet together [F(1,67) = 5.421, P = 0.0229] but not eyes open and feet apart [F(1,67) = 0.177, P = 0.68]. These interactions indicated disproportionately higher quotients in the alcoholics relative to controls in the anterior-posterior direction relative to the medial-lateral direction of the feet together conditions.

Inspection of Figure 3, presenting spectral analysis of sway path velocity, revealed additional power above 5 Hz, greater in alcoholics than controls, followed by a diminishing of group differences thereafter. The most prominent group differences were present when comparing the power in a 5–7 Hz band for feet apart versus feet together with eyes closed [group × vision interaction, F(1,67) = 7.526, P = 0.0078]. The group differences fully dissipated with eyes open and feet apart.

Group Differences in Regional Brain Volumes

The alcoholic group did not have significant vermian volume deficits as defined by the current control group, but the alcoholic group did have volume deficits in cerebellar hemispheres and supratentorial gray matter. Despite the absence of a statistically significant group difference in vermian volumes, 19 of 39 (49%) alcoholics had volumes below the control mean and 12 alcoholics (31%) had at least a 0.5 SD volume deficit relative to controls (Fig. 4).

Correlations with Cerebellar Vermian and Comparison Brain Volumes

In alcoholics, but not controls, smaller vermian volumes correlated with longer sway paths in all conditions; five of the eight correlations were statistically significant (P < 0.022). The most robust correlations were with eyes open, feet together with (r = -0.38, P = 0.0173) and without (r = -0.48, P = 0.0022)
A multiple regression analysis used a pair of composite sway path scores — the mean of all four conditions with eyes open and the mean of the eyes closed conditions — and entered them as simultaneous predictors of vermian volume. Although each composite score correlated with vermian volume (eyes open $r = -0.44$, $P < 0.006$; eyes closed $r = -0.33$, $P < 0.04$), the eyes open composite score had a unique relation with vermis ($P = 0.05$) over and above the contribution from the eyes closed composite score ($P = 0.53$). An analogous multiple regression analysis based on a pair of composite scores contrasting the feet together and feet apart conditions failed to identify either composite as having a unique relation to vermian volume.

In no case did longer sway path length correlate with smaller volumes of the cerebellar hemispheres or supratentorial cortical gray matter or with area of the corpus callosum in either the alcoholics or the controls. To test selectivity of the vermillion-based correlations with respect to the cerebellum, multiple regression analyses entered volumes of the vermis and the cerebellar hemispheres as simultaneous predictors of sway path length. In no case was cerebellar hemisphere volume a unique predictor of sway path length ($P > 0.31$), whereas vermian volume was a unique predictor in five conditions: EC--FA--NoTch ($P = 0.0372$), EC--FT--Tch ($P = 0.0766$), EO--FA--NoTch ($P = 0.0403$), EO--FT--NoTch ($P = 0.0084$) and EO--FT--Tch ($P = 0.0553$).

The frequency ratios (2–5Hz/0–2) under six balance conditions (irrespective of the touch cue) correlated significantly with vermian volume but not other brain volumes measured. Four of the six correlations were based on the anterior–posterior direction (eyes closed/feet together $r = -0.38$, $P = 0.0159$; eyes open/feet together $r = -0.35$, $P = 0.0296$;
eyes closed with feet apart $r = -0.37$, $P = 0.0191$; eyes open with feet apart $r = -0.35$, $P = 0.0284$) and two in the medial-lateral direction (eyes closed with feet together $r = -0.34$, $P = 0.0329$; eyes open with feet together $r = -0.47$, $P = 0.0027$). None of the correlations of the 5–7 Hz power band and vermian volume was statistically significant.

Figure 4. Examples of cerebellar morphology in a 56 year-old alcoholic (left) and a 61-year old control. The left column for each subject contains T1-weighted SPGR images; the right column contains late echo FSE images. Note that the alcoholic man has a 1.3 SD volume deficit (for his intracranial volume (ICV) and age) in the anterior superior vermis, whereas the control man’s volume is representative of normal for ICV and age.

Figure 5. In alcoholics, smaller vermian volumes correlated with longer sway paths: eyes open, feet together, with ($r = -0.38, P = 0.0173$) and without ($r = -0.48, P = 0.0022$) touch cues.

Correlations with Alcoholism Variables
In the alcoholics, lifetime alcohol consumption did not correlate with any of the balance measures, but length of sobriety did. When including only the 34 alcoholics who had been sober for a maximum of 128 days, longer sobriety duration predicted shorter sway paths, especially notable in the feet apart
conditions \((r = -0.46, P = 0.0063)\) (Fig. 6). Multiple regression analysis entering vermian volumes and sobriety length as predictors of sway indicated that vermian volume \((P = 0.0007)\) and length of sobriety \((P = 0.0003)\) were each independent predictors of sway path in the feet apart conditions.

Length of sobriety also correlated with the power of sway velocity spectrum (irrespective of sway direction) for the 2–5/0–2 Hz ratio and the 5–7 Hz frequency band. Of particular importance was the differential pattern of variance shared between vermian volume and length of sobriety in the two power of sway velocity spectrum measures detected with multiple regression analysis. In three of four analyses, vermian volume endured as a significant unique predictor of the 2–5/0–2 Hz ratio over and above the contribution from sobriety length (EC–FA: \(r^2 = 0.16\), vermis \(P = 0.023\), sobriety \(P = 0.78\); EC–FT: \(r^2 = 0.22\), vermis \(P = 0.0061\), sobriety \(P = 0.67\); EO–FA: \(r^2 = 0.07\), vermis \(P = 0.17\), sobriety \(P = 0.68\); EO–FT: \(r^2 = 0.26\), vermis \(P = 0.0029\), sobriety \(P = 0.26\)). By contrast, length of sobriety and vermian volume each contributed uniquely to observed power in the 5–7 Hz band, with the contribution relatively greater by sobriety length than vermian volume in three instances (EC–FA: \(r^2 = 0.39\), vermis \(P = 0.0046\), sobriety \(P = 0.0007\); EC–FT: \(r^2 = 0.16\), vermis \(P = 0.14\), sobriety \(P = 0.0354\); EO–FA: \(r^2 = 0.24\), vermis \(P = 0.0592\), sobriety \(P = 0.0088\); EO–FT: \(r^2 = 0.25\), vermis \(P = 0.0188\), sobriety \(P = 0.019\)).

**Discussion**

The first goal of this study was to establish *in vivo* MRI evidence for a selective cerebellar vermian substrate of static postural control determined with physiological and quantitative measures of center-of-pressure sway path and postural tremor. The results indicated a vermian volume–sway path relationship that was selective, in that it was (i) greater than that with volume of the cerebellar hemispheres, cerebral cortex, or corpus callosum; (ii) not attributable to length of sobriety; and (iii) specific to conditions with eyes open rather than eyes closed. Traditionally, exaggerated sway with eyes closed has been considered a characteristic of posterior column lesions (Adams and Victor, 1989; Lanska and Goetz, 2000), although patients with focal cerebellar lesions can also manifest this effect (Mauritz et al., 1979; Baloh et al., 1998). Conversely, the present analysis provided evidence for a vermian substrate of compromised postural control that endures with vision. Although quantitative information about presence of peripheral neuropathy was not available for the alcoholics, a prior study rigorously examined the potential influence of alcohol-related peripheral neuropathy on postural sway in a group of 78 chronic alcoholics and found no correlation between degree of neuropathy and severity of cerebellar ataxia in alcoholics (Scholz et al., 1986). Thus, even if peripheral neuropathy were present in our alcoholics, it did not prevent the alcoholics’ ability to take advantage of sensorimotor cues to normalize the observed physiological signs of tremor and exaggerated sway observed when cues were absent.

In this study sample, the alcoholic group did not have significant vermian volume deficits as defined by the current control group, but the alcoholic group did have volume deficits in cerebellar hemispheres and supratentorial gray matter. Despite the lack of defined vermian volume deficit, the alcoholics but not the controls showed the expected correlation between sway and vermian volume; further, this relation was selective to the vermis and was not accounted for by concurrent volume deficits in the cerebellar hemispheres or supratentorium.

The alcoholics exerted significantly less control than the controls when maintaining erect posture in the absence of visual, tactile, or stance cues. Although longer sobriety was predictive of shorter sway paths, residual excessive sway without stabilizing cues was still measurable months after cessation of drinking. In the presence of cues, however, the sway paths of the patients were indistinguishable from those of the controls, indicating that the alcoholics had functionally adequate sensorimotor integration skills despite the likely cerebellar basis for impaired postural control. The power of the sway velocity spectrum in the 2–7 Hz frequencies was also greater in patients than controls and may be related to poor control of trunk orientation, but postural tremor at all of these frequencies was ameliorated with sensorimotor cues.

Differences in stance width may be considered more a biomechanical aid than a sensory aid or cue for mitigating postural sway. Changing from a narrow- to a broad-based stance invokes a change in balance strategy from hip to trunk (Day et al., 1993). Narrow stance has been shown to invoke postural control via the trunk (Winter et al., 1998). Lesion studies have shown that truncal control of quiet standing is disrupted by spinocerebellar pathology (Dichgans and Diener, 1989; Hirayama et al., 1994; Van de Warrenburg et al., 2005), which is consistent with the correlations noted in the present study between exaggerated sway paths and vermian volume.

Neurological and other experimental accounts indicate that sway in patients with vermian lesions, including detoxified alcoholics, occurs preferentially in the anterior–posterior plane (Mauritz et al., 1979; Baloh et al., 1998). Lifetime alcohol consumption in alcoholics has also been related to posturographic measures of anterior–posterior but not medial–lateral static postural control with or without visual input (Wober et al., 1999; Ahmad et al., 2002). Although this selective directional relationship was not substantial in the sway path lengths of the present study, the frequency analysis of
sway velocity provided robust support for a preferential anterior-posterior sway in the alcoholic group compared with sex- and age-matched controls, especially in the 2-5 Hz frequency range.

Prior balance platform studies of recovering alcoholics report enduring instability measurable with static posturography (Victor et al., 1981; Brown et al., 1997). In addition to abnormally greater sway velocity in this frequency band, however, abnormal sway velocity power also occurred at 5–7 Hz in our patients and may have arisen from compromise of cerebellar-thalamic structures and circuitry (cf. Middleton and Strick, 1997; Schmahmann and Pandya, 1997). Support for this possibility derives from an animal model of parkinsonism (Deuschl et al., 1998), showing that a lesion in thalamic nuclei receiving input from the cerebellum produced postural tremor at 5–7 Hz that was exquisitely sensitive to sensory input, which served to quell the tremor in affected animals. Also consistent with the cerebellar circuitry hypothesis is a set of observations made in three cases of axial postural tremor with suspected or autopsy-confirmed cerebellar pathology (Brown et al., 1997; Sullivan et al., 2000b; Rosenbloom et al., 2004). Indeed, that was the case for the patients in the present study when tested without the advantage of cues.

The frequency of cerebellar kinetic or postural tremor occurs at 3–5 Hz (Gilman et al., 1981; Brown et al., 1997). In addition to abnormally greater sway velocity in this frequency band, however, abnormal sway velocity power also occurred at 5–7 Hz in our patients and may have arisen from compromise of cerebellar-thalamic structures and circuitry (cf. Middleton and Strick, 1997; Schmahmann and Pandya, 1997). Support for this possibility derives from a model of parkinsonism (Deuschl et al., 1998), showing that a lesion in thalamic nuclei receiving input from the cerebellum produced postural tremor at 5–7 Hz that was exquisitely sensitive to sensory input, which served to quell the tremor in affected animals. Also consistent with the cerebellar circuitry hypothesis is a set of observations made in three cases of axial postural tremor with suspected or autopsy-confirmed cerebellar pathology (Brown et al., 1997). These patients displayed tremor at frequencies varying between 3 and 10 Hz that was attributed to cerebellar pathology and compromised outflow pathways. Although clinically detectable tremor and movement disorders are associated with alcoholism-based hepatic dysfunction (e.g. asterixis, metabolic tremor) and with alcohol withdrawal (e.g. transient parkinsonism) (Neiman et al., 1990), the alcoholics in the present study exhibited no signs of liver disease and were well beyond the acute phase of withdrawal. Thus, we speculate that neural substrate of the impaired postural control and associated increased power of the velocity spectrum up to 7 Hz in our alcoholics was compromise of the anterior superior vermian lobules together with disruption of cerebellar-pontine-thalamic circuitry known to occur in uncomplicated alcoholism (Sullivan, 2003; Sullivan et al., 2003).

In conclusion, sway path length was selectively related to volume of the cerebellar vermis and not the lateral cerebellar hemispheres, thus providing correlational evidence for functional differentiation of these cerebellar regions (cf. Herrup and Kuemerle, 1997). Further substantiation for a vermian mechanism of excessive sway derived from spectral frequency analysis, which revealed associations of smaller vermian volume with greater power of the velocity spectrum. A secondary tremor prominence was present in the 5–7 Hz band, previously underappreciated with respect to postural control. Without sensorimotor cues, the sway paths of the alcoholics were ~30% longer than those of the controls, thus putting these individuals at heightened risk of falling when under sensorimotor impoverished conditions. Improvement to normal levels in balance and reduction in sway and tremor with the introduction of sensory information and broad-based stance provide evidence that adaptive mechanisms involving sensorimotor integration can be invoked to compensate for CNS-related deficits in static balance.

**Notes**

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