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Postural sway reduction in aging men and women: Relation to brain structure, cognitive status, and stabilizing factors

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Abstract

Postural stability becomes compromised with advancing age, but the neural mechanisms contributing to instability have not been fully explicated. Accordingly, this quantitative physiological and MRI study of sex differences across the adult age range examined the association between components of postural control and the integrity of brain structure and function under different conditions of sensory input and stance stabilization manipulation. The groups comprised 28 healthy men (age 30–73 years) and 38 healthy women (age 34–74 years), who completed balance platform testing, cognitive assessment, and structural MRI. The results supported the hypothesis that excessive postural sway would be greater in older than younger healthy individuals when standing without sensory or stance aids, and that introduction of such aids would reduce sway in both principal directions (anterior–posterior and medial–lateral) and in both the open-loop and closed-loop components of postural control even in older individuals. Sway reduction with stance stabilization, that is, standing with feet apart, was greater in men than women, probably because older men were less stable than women when standing with their feet together. Greater sway was related to evidence for greater brain structural involutional changes, indexed as ventricular and sulcal enlargement and white matter hyperintensity burden. In women, poorer cognitive test performance related to less sway reduction with the use of sensory aids. Thus, aging men and women were shown to have diminished postural control, associated with cognitive and brain structural involution, in unstable stance conditions and with diminished sensory input.

Keywords

Postural control; Posturography; Balance; Cerebellum; Brain; MRI; White matter hyperintensity; Sway; Age; Sex

1. Introduction

Upright stance, which typically becomes less stable with older age (Baloh et al., 2003; Collins et al., 1995; Rogind et al., 2003), is controlled by multiple factors. In addition to mechanical

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contributions from musculoskeletal and joint systems (for reviews, Butler et al., 2006; Winter et al., 2003), postural stability in normal healthy adults is affected by the availability and validity of visual, vestibular, haptic, and proprioceptive information that can provide a referential context for updating the body's location in extrapersonal space (Horak, 2006; Jeka and Lackner, 1994; Lackner and DiZio, 2005; Leibowitz and Shupert, 1985; Peterka and Loughlin, 2004). Useful integration of these informational sources depends, at least in part, on the integrity of brain structure and function and can be disturbed (Coppin et al., 2006; Shumway-Cook et al., 1997; Slobounov et al., 2005; Stelmach and Worringham, 1985) or enhanced (Rankin et al., 2000; Weeks et al., 2003) by cognitive factors. Failure to take advantage of stabilizing information can result in falling, which is one of the leading causes of morbidity and mortality in otherwise healthy aging individuals (Radebaugh et al., 1985; Tinetti et al., 1995a,b; Tinetti and Williams, 1998). Given the multifaceted nature of factors contributing to upright stance, efforts to identify mechanisms that can induce or ameliorate age-related postural instability require concurrent examination of these multiple variables.

Quantitative assessment of static posture with a balance platform provides opportunities to parse component processes of the postural control system and to test factors that influence balance (Bortolami et al., 2006; Collins and De Luca, 1993; Collins et al., 1995; Norris et al., 2005). The balance platform provides information on the center of pressure trajectory of an individual while standing and maintaining erect posture. The resultant data, rendered in a sway path stabilogram, represent the changes in pressure in two dimensions—anterior–posterior and medial–lateral. The length of the sway path over time is a classical measure of postural control. Another analysis approach is based on statistical biomechanical concepts, which treat the stabilogram as a system of coupled, correlated random walks that can be characterized by a diffusion coefficient.

As applied to the maintenance of erect static posture, the diffusion coefficient plot of successive temporal interval displacements devised by Collins and colleagues (Collins and De Luca, 1993, 1995b; Collins et al., 1995) reveals two distinct components, a short-term (i.e., short time interval, usually less than 2 s) and a long-term (i.e., greater than 2 s) component. The short-term component behaves like an open-loop control system that is mostly devoid of feedback, whereas the long-term component behaves like a closed-loop system with feedback based on afferent input. The open-loop component of postural control is little affected by attentional or other cognitive processes and is characterized by a steep-sloped activity gradient (Collins and De Luca, 1995b; Diener et al., 1989; Jeka et al., 1997). While brief, this component is prolonged in older relative to younger healthy individuals and can be a source of instability. The closed-loop component can be affected by internal and external perceptual information and cognitive demands (Raymakers et al., 2005) and typically has a long, relatively flat-sloped activity gradient, little affected by age (Collins et al., 1995). The steeper the slope of the diffusion plot components, the less tightly regulated and more random the control mechanisms. We used this diffusion model to parse the sway path in an effort to determine the extent to which age-related prolongation of the open-loop component could be shortened with sensory information and whether evidence for improvement in stability was related to measures of brain structural or functional integrity.

Brain dysmorphology associated with excessive sway in normal elderly individuals include ventricular enlargement and white matter hyperintensities (WMHI) (Tell et al., 1998), which typically occur in subcortical and periventricular brain regions (DeCarli et al., 2005; Jernigan et al., 1991). An early computed tomography study reported that elderly prone to falling had greater evidence of white matter disease than an age-matched group not prone to falling (Masdeu et al., 1989). More recent magnetic resonance imaging (MRI) studies report associations between WMHI burden and balance instability in older community-dwelling individuals (Guttmann et al., 2000; Starr et al., 2003; Tell et al., 1998), even when screened

for cognitive impairment (Baloh et al., 2003). While nonspecific, both neuroradiological signs are markers of structural degradation occurring with normal aging and are also concomitants of declining cognitive function (DeCarli et al., 2001; Garde et al., 2000; Gunning-Dixon and Raz, 2000; Raz et al., 2007) or processing speed (Nebes et al., 2006; Schmidt et al., 1993; van den Heuvel et al., 2006). Which components of sway are associated with these brain markers of decline and whether sway during quiet standing can be ameliorated by sensory information and stance stabilization in healthy elderly with age-related ventricular or sulcal expansion or WMHI burden remain unanswered.

In addition to nonspecific brain correlates of impaired stability, specific correlates have been documented. For example, postural balance is impaired in individuals with pathology of the anterior superior vermis of the cerebellum, which is most commonly caused by chronic alcoholism [neuropathological evidence: Baker et al., 1999; Harper and Kril, 1993; Victor et al., 1989 and neuroimaging evidence: Gilman et al., 1990; Martin et al., 1995; Sullivan et al., 2000; Sullivan et al., 2006]. Functional imaging studies using positron emission tomography (PET) and single photon emission computed tomography (SPECT) have revealed activation of the cerebellar vermis in healthy, nonalcoholic men and women when engaged in postural control tasks. A PET activation study conducted after posturography was recorded in healthy adults assuming five different positions – from supine to sitting to standing – revealed greater regional blood flow in the anterior superior lobules of the vermis in participants with greater balance control while standing (Ouchi et al., 1999, 2001). Whether age-related decline in vermician volume is associated with postural instability or contributes to the more general indices of brain integrity (that is, WMHI and ventricular size) is not established.

The purpose of our study was to identify which component processes of static balance are differentially disrupted in healthy adults as they age. In addition, we tested whether identified components of imbalance could be ameliorated by external sensorimotor visual, tactile, and stance factors known to exert stabilizing forces in normal, healthy adults. Accordingly, 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 (McCollum et al., 1996; Nashner and Peters, 1990; Sullivan et al., 2006). We tested the hypothesis that excessive postural sway would be greater in older than younger healthy individuals when standing without sensory or stance aids, and that introduction of such aids would reduce sway in both principal directions (anterior–posterior and medial–lateral) and in both the open-loop and closed-loop components of postural control even in older individuals. We also examined whether men and women would differ in ability to reduce sway with sensory aids or change in stance. Finally, we tested whether (1) greater sway related to greater evidence for brain structural degradation, indexed as ventricular and sulcal enlargement and WMHI burden and specifically as volume of the anterior superior vermis, that is, brain measures previously shown to predict postural instability in health or with CNS injury, and (2) poorer cognitive test performance related to ability to use sensory aids to reduce sway. Identification of factors that mitigate falling liabilities in the elderly could reduce age-related disability, which can be costly, curtail normal activities, and diminish quality of life.

2. Methods

2.1. Subjects

The groups comprised 28 men (age 30–73 years) and 38 women (age 34–74 years), recruited from the local community. All subjects underwent a psychiatric interview and medical history to identify the following exclusionary criteria: presence of DSM-IV (APA, 1994) Axis I diagnoses of bipolar disorder or schizophrenia, history of substance abuse or dependence, CNS trauma (such as loss of consciousness for greater than 30 min, seizures, degenerative disease),

or serious medical condition (such as insulin-dependent diabetes, hepatic disorder). All subjects were volunteers, gave written informed consent, obtained according to the Declaration of Helsinki and the Ethical Committees of Stanford University School of Medicine and SRI International, to participate in this study and were paid a modest stipend for participation. The men had served as healthy controls in our previous study of alcoholic men using the same balance platform paradigm (Sullivan et al., 2006).

The men and women did not differ significantly in age, handedness, education, socioeconomic status, or intelligence estimated with the National Adult Reading Test (Nelson, 1982) or Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999). All subjects were within the normal ranges on two screening tests for dementia, the Mini-Mental Status Examination (Folstein et al., 1975) and the Dementia Rating Scale (Mattis, 1988). The men had a greater body mass index (BMI) than the women ($t(64) = 2.217, p = .0302$) and had drunk more alcohol over their lifetimes than the women ($t(59) = 3.062, p = .0033$), but no participant met DSM-IV-R or alcohol consumption criteria for alcohol abuse or dependence. Table 1 presents these demographic data separately for the men and women.

Participants age 65 years or older comprised 21% of the group (14 of 66). The age range of the total group was 30–74 years, and the percentages by decade were as follows: 18% for the 30s, 23% for the 40s, 21% for the 50s, 27% for the 60s, and 11% for the 70s (for which the oldest age was 74). Given these percentages, the sample sizes well represented the decades examined and did not over-represent younger adults.

According to self-report, seven participants had high blood pressure and six of those seven were on antihypertensive medication; the one not on one medication was seen in follow-up and declared that her physician said she was not hypertensive. No subject reported having had classical migraine, diabetes mellitus, or childhood diabetes. One index of cardiovascular health is body mass index (BMI), which did not correlate significantly with age ($r = .06, p = .61$); nonetheless, 11 individuals had $BMI \geq 30$, which is considered “obese” by the National Heart, Lung, and Blood Institute, and all were over 60 years old.

To test for the presence of parkinsonian signs, we obtained quantitative data on grip strength and fine finger movements. We divided the controls into groups based on age decades (30–39, ..., 70–74 years) and conducted one-way ANOVAs for each motor measure over the five subgroups (five decades). Neither unimanual nor bimanual fine finger movement output was significantly different across the groups nor was grip strength for either hand (p -values ranged from .279 to .994). Examination of the individual data points confirmed the absence of outliers (with low fine finger movement output or poor grip strength) in any age group.

Most subjects (73% of men and 67% of women) were also interviewed to obtain a history of falls experienced over the past year (Tinetti et al., 1995a,b) and reported not falling. Of the 22 men questioned, only 1 fell more than once over the past year; of the 30 women questioned, 4 recalled falling twice and 1 reported falling 4 times. Younger participants were as likely to report falls as older ones.

2.2. Posturography

2.2.1. Sway path analysis—As described previously (Sullivan et al., 2006), balance was assessed with a microcomputer-controlled force plate measurement device (model 9284; Kistler, Amherst, NY, USA) with multiple transducers and analog-digital converters. The data were sampled at 50 Hz, and the resultant native data were 30-s trials of 1500 center of pressure displacements (x and y pairs). The sway path length was expressed as the line integral following 10 Hz non-recursive lowpass filtering (seven terms, -50 db Gibbs).

2.2.2. Analysis of sway path components—We applied the stabilogram-diffusion analysis of Collins and colleagues (Collins and De Luca, 1993; Collins et al., 1995) to compute the characteristics of open-loop (short-term) and closed-loop (long-term) control mechanisms. The first step was the computation of the average square planar displacement (pd^2) across the entire data set computed for 499 time intervals (m) from .02 to 10 s in .02 s increments. Thus, the average squared displacement (pd^2) was computed for all pairs of points separated sequentially by .02 s for the first interval, .04 s for the second, .06 s for the third, ..., 10 s for the 499th.

Three diffusion plots were created (y-axis = anterior–posterior displacement, x-axis = medial–lateral displacement, and xy = average squared radial displacement) with the 499 displacements plotted against the 499 time intervals. The plots were then fit with two separate linear components, the short-term diffusion coefficient (D_S) reflecting the open-loop characteristics and the long-term diffusion coefficient (D_L) reflecting the closed-loop characteristics. The critical point was the time interval at which the two linear components intersected. The dependent variables from these analyses were D_S = one half the slope of the linear fit of the open-loop component and D_L = one half the slope of the linear fit of the closed-loop component.

2.2.3. Test conditions—The six experimental conditions of static balance were visual (eyes open or closed), stance (feet apart or feet together), and touch (touch or no touch). These conditions yielded eight combinations, which for data reduction were made into three composite scores by taking the mean sway path lengths of the three conditions that included the named composite: feet together, feet apart, eyes closed, eyes open, no touch, and touch. 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. Fig. 1 presents examples of sway paths without any aids and with three aids.

2.3. MRI and DTI acquisition and analysis

All participants underwent MRI structural scanning. Prior to quantitative analysis, images were read by a clinical neuroradiologist to exclude any subjects with space occupying lesions or other dysmorphology that would be indicative of neuropathology other than the target conditions or that would interfere with morphometric analysis.

2.3.1. MRI acquisition protocol—Three coronal structural sequences were used for this analysis: (1) a SPoiled Gradient Recalled Echo (SPGR) sequence (94 slices, 2 mm thick; TR/TE = 25/5 ms, flip angle = 30°, matrix = 256 × 192), (2) a thin-slice, late-echo fast spin echo (TFSE) sequence at the same slice locations as the SPGR (94 slices, 2 mm thick; TR/TE = 11,050/98 ms, matrix = 256 × 192), (3) a Fluid Attenuated Inversion Recovery (FLAIR) sequence (47 contiguous slices, 4 mm thick; TR/TE/TI=9000/82.5/2200 ms; matrix=256 × 192). The FLAIR acquisition was prescribed with custom software, such that each 4 mm slice precisely encompassed a pair of 2 mm thick TFSE slices, and the FLAIR data were upsampled from 47 to 94 slices. All images were zero-filled to 256 × 256 pixels in-plane by the scanner reconstruction software. All data were resampled to 1 mm isotropic voxels.

2.3.2. Atlas-based parcellation of the ventricles—The third and lateral ventricles were manually identified in our laboratory on a high-resolution, low-noise template brain (Collins et al., 1998). The lateral ventricles were divided into left and right, temporal horn, anterior (anterior to the ante rior commissure), middle, and occipital portions. The SPGR data from each subject were aligned with a template brain in a two-step process (Pfefferbaum et al.,

2007). The template brain with skull was aligned to each subject's brain with skull with a nine-parameter affine transformation followed by nonrigid alignment (multi-level, third-order B-spline, with 5-mm final control point spacing; Rohlfing and Maurer, 2003; Rueckert et al., 1999). Applying the deformed template brain mask (derived with FSL-BET; Smith, 2002) to each subject's native data produced a robust brain stripping. A second registration pass (starting with initial affine followed by a second nonrigid) aligning the stripped template brain to the stripped brain of each subject produced the final registration. This final registration was then applied to warp the manual parcellation of the template brain (lateral and third ventricles, and temporal horn) onto each subject's native brain, producing subject-specific labeled brain structures (Fig. 2).

2.3.3. Atlas-based parcellation of supratentorial brain tissue and CSF—The TFSE sequence produced high contrast CSF/tissue conspicuity and is particularly suited for identification of the intracranial volume because of the high signal of sulcal CSF adjacent to the low signal of dura and skull. Because TFSE data were not available for the SPGR low-noise template brain, a separate TFSE template was created using the data of a control subject (52-year-old man). It was skull stripped with FSL-BET and the supratentorial volume identified manually, excluding the posterior fossa, pons and brain stem. The same two-step registration process used for the SPGR data was used for the TFSE data and TFSE template. The final registration then applied the parcellated TFSE template brain to each subject, producing an intracranial volume and a supratentorial volume for each subject. A non-parametric histogram segmentation operator (Lim and Pfefferbaum, 1989) was applied to the supratentorial volume for each subject, yielding supratentorial tissue and CSF volumes (Fig. 2). Given the closed space of the supratentorium, representing the maximal size of brain growth, as brain tissue shrinks with age, it is replaced with CSF.

2.3.4. White matter hyperintensity (WMH) quantification—The supratentorial volume from the TFSE parcellation was projected onto the FLAIR data. All voxels below the AC–PC plane were eliminated, and those superior to this plane were treated with an erode morphological operator to remove the outer 2 cm of the volume to produce a subcortical volume (Fig. 2). An intensity histogram of this volume was fit with a six-term Gaussian function, and the number of voxels with an intensity exceeding 3 S.D. was considered WMH burden.

2.3.5. Cerebellar anterior superior vermis—Cerebellar morphometric quantification was based on a semi-automated segmentation of the TSFE data, which 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 re-aligned 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 (Courchesne 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 (Fig. 2). All scoring was conducted manually and blind to subject identification.

2.4. Statistical analysis

The sway path data were subjected to repeated measures analyses of variance (ANOVAs) and *t*-tests. Vision and touch are perceptually based aids, whereas changes in stance width (that is, standing with feet apart or feet together) exert biomechanical effects on postural stability (Winter et al., 1998, 2001). Therefore, initial ANOVAs focused on the effects of vision and touch aids in the feet-apart conditions and separately in the feet-together conditions. Where appropriate, Geiser–Greenhouse correction was applied. Correlations between sway path

lengths and demographic factors or cognitive performance or regional brain volumes were tested with Pearson correlations. Multiple regression analysis was used to test for specificity of relationships.

3. Results

3.1. Sway path length and direction: effect of vision, touch, and stance

3.1.1. Sex differences in use of vision and touch aids—Two separate repeated measures ANOVAs (two group $\times$ two touch conditions $\times$ two vision conditions) compared aided versus unaided performance (1) with feet together and (2) with feet apart (Fig. 3). Regardless of stance, sway paths were significantly shorter with vision or touch aids than without these aids ($p = .0001$ for all comparisons). A group-by-visual aid interaction indicated that men tended to have disproportionately longer sway paths with eyes closed than open relative to women ($F(1, 64) = 3.464, p = .0673$).

3.1.2. Sex differences in stance and sway direction—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 aids. A repeated measures ANOVA for group, condition, and direction yielded a three-way interaction ($F(1, 64) = 7.194, p = .0093$), indicating that sway was greater in the anterior–posterior direction than the medial–lateral direction with feet apart but the opposite occurred with feet together; further, the improvement in sway from feet together to feet apart was greater in the men than women, especially for medial–lateral sway (Fig. 4).

Neither directional component of sway path length was correlated with age in the women but both were in the men. Standing with feet apart, sway paths of men tended to increase with age in the anterior–posterior ($r = .37, p = .0532$) but not the medial–lateral direction ($r = .05, p = .81$). Standing with feet together, sway paths of men increased with age in both the medial–lateral ($r = .50, p = .0071$) and anterior–posterior directions ($r = .49, p = .0075$).

3.1.3. Effect of practice or 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 by three-trial ANOVAs were sought for each set of aided conditions. In no condition did men or women show significant practice or fatigue effects across the three trials.

3.2. Correlations between sway path length and age

For all correlational analyses – age, brain measures, and neuropsychological performance – men and women were examined separately because of the sex differences observed in the sway conditions. To reduce the number of correlations tested between sway path lengths and age or other factors, we created composite scores, yielding six summary conditions: eyes open, eyes closed, touch, no touch, feet apart, and feet together. Each composite score was the mean of the sway paths using that condition (for example, eyes open = mean of the four sets of trials requiring the eyes to be open).

For all composites for both sexes, longer sway paths correlated with older age using a linear fit (Fig. 5 for scatterplots by sex, correlation coefficients, and p -values), although not all correlations were significant. The correlations were generally greater for men than women, but in no case did the age correlations differ between men and women. Nonetheless, older men exhibited disproportionately great sway with their feet together relative to feet apart (difference between slopes of the age regressions: $t(25) = 6.191, p = .0001$) and without touch aids relative to presence of touch aids (difference between slopes of the age regressions: $t(25) = 2.081, p$

= .0478). Unlike the men, the women did not show this exacerbation of sway with age under sensorily or motorically challenged conditions. These correlations and differences endured when excluding a 72-year-old man and a 78-year-old woman because of their exceptionally long sway paths.

We also calculated a sway-reduction index, which was the difference in sway path length between the most challenging condition (noaids: eyes closed/no touch/feet together) and the least challenging condition (three aids: eyes open/touch/feet apart) divided by the least challenging condition. A greater sway-reduction index correlated significantly with older age in the men ($r = .54, p = .0028$) but not the women ($r = .16, p = .3465$) (Fig. 6), and the difference between these correlations was significant ($z = 1.69, p = .0455$, one-tailed).

3.3. Correlations of sway path lengths with MRI regional brain volumes and WMHI index

These analyses were conducted without data from the man and woman with the exceptionally long sway paths. These subjects were statistical outliers that inflated several of the correlations between sway path and age. Rather than using nonparametric analyses, we chose to exclude these subjects to enable use of multiple regression analysis without special bias, which would actually have been in favor of predicted results.

In neither the men nor the women did size of the vermis correlate significantly with any sway path composite measure for feet apart or together. For correlations significant at $p \leq .05$, men and women showed different patterns. For men, although both volumes of the lateral ventricular body and supratentorial CSF correlated with each of the six sway path composite scores, multiple regression analysis indicated that only supratentorial CSF volume persisted as a significant independent predictor of sway for five of the six composite scores (eyes open $t(26) = 2.41, p = .0243$; eyes closed $t(26) = 2.84, p = .0093$; feet apart $t(26) = 2.71, p = .0126$; feet together $t(26) = 2.42, p = .0238$; touch $t(26) = 1.65, p = .1122$; no touch $t(26) = 3.51, p = .0019$). Fig. 7 displays the simple regressions between supratentorial CSF volume and sway path lengths in the men. In the women, only the WMHI index correlated consistently with the sway path lengths (Fig. 8).

Additional multiple regression analyses used measures from the pair of sway path conditions used in the sway-reduction index – no aids (eyes closed/no touch/feet together) and three aids (eyes open/touch/feet apart) – and entered them as simultaneous predictors of the brain MRI measures. In the men, the no-aid ($t(26) = 3.14, p = .0044$) but not the three-aid condition ($t(26) = .499, p = .6223$) was independently related to supratentorial CSF volume; together these variables account for 34% of the variance. For the women, the three-aid but not the no-aid condition was independently related to the posterior ($t(35) = 2.42, p = .0213$) and third ventricular ($t(35) = 2.74, p = .0099$) volumes, supratentorial CSF volume ($t(35) = 3.14, p = .0075$), and the WMHI index ($t(35) = 2.02, p = .0518$). Multiple regression analysis examined potential independent contributions of age and supratentorial CSF volume to the sway-reduction index in the women and revealed that age ($t(35) = 2.43, p = .021$) and supratentorial CSF volume ($t(35) = 3.31, p = .0023$) each made significant contributions to the overall variance and together accounted for 27% of it.

Although age and obesity are cardiovascular risk factors, BMI did not correlate with the WMHI index ($r = .02, p = .86$). Further, neither BMI nor age emerged as a significant, independent predictor of the WMHI index in a simultaneous multiple regression analysis.

3.4. Correlations of sway path lengths with cognitive performance and other factors

Poorer cognitive performance correlated with longer sway paths in the women but not the men. For the women, Dementia Rating Scale scores were consistently correlated with sway

composites with sensory or stance aids: feet apart $r = -.47$, $p = .0049$; eyes open $r = -.39$, $p = .023$; touch $r = -.43$, $p = .0108$ (Fig. 9). Neither the men nor the women showed correlations between sway path length and years of education or estimated lifetime consumption of alcohol.

3.5. Short-term versus long-term components of static postural control: sex differences and correlations with age and MRI measures

A series of repeated measures ANOVAs (sex by open-loop versus closed-loop components) sought interactions between sex and slopes of the short-term (open-loop) versus long-term (closed-loop) components, but none was forthcoming. The only systematically significant effects were between the slopes of the short-term component, which were steep, and the relatively flat slopes of the long-term components ($p = .0001$ in all cases). Additional differences were notable between the most challenging condition (eyes closed/no touch/feet together) and the least challenging condition (eyes open/touch/feet apart), where $p = .0001$ for the short-term and long-term component ANOVAs (Fig. 10). Analysis of the critical point (that is, the intersection of the short- and long-term slopes) of the most and least challenging conditions revealed a sex-by-condition interaction ($F(1, 64) = 5.076$, $p = .0277$) but no effect of sex per se ($F(1, 64) = .0102$, $p = .9197$). The interaction indicated that the average time that women switched from open- to closed-loop control was shorter in the difficult than easy condition, whereas the opposite pattern described the switch by the men.

Despite absence of sex differences in short-term or long-term slopes, men and women differed in the effect of age on components of sway control. Whereas none of the age–summary score correlations was significant in the women, the men exhibited effects, which were restricted to the short-term component, where steeper slopes correlated with older age: eyes closed $r = .44$, $p = .0199$; eyes open $r = .42$, $p = .025$; no touch $r = .49$, $p = .0089$; touch $r = .32$, $p = .0932$; feet together $r = .43$, $p = .0227$; feet apart $r = .40$, $p = .0337$. The men showed similar correlations between steeper short-term component slopes and supratentorial CSF volumes: eyes closed $r = .46$, $p = .0142$; no touch $r = .46$, $p = .014$; feet together $r = .39$, $p = .0431$; feet apart $r = .48$, $p = .0104$.

Finally, we conducted two group comparisons (parametric t -tests and nonparametric Mann–Whitney tests) to examine whether balance scores or regional brain measures differed between subjects reporting high blood pressure and those not and between subjects taking such medications versus those not taking them. In neither case did the groups differ in sway path length or the target MRI measures of vermian volume, supratentorial CSF, or WMHI index.

4. Discussion

Sex, age, cognitive status, and brain integrity each made differential contributions to selective components of postural stability maintenance in healthy adults. How each of these factors related to static balance is considered in turn.

4.1. Sex and age differences in maintaining postural stability

Vision and touch sensory aids reduced sway in both stance conditions. With the exception of modestly greater sway in men than women when standing quietly with eyes closed, men and women performed similarly (cf. Rogind et al., 2003). Changing from a narrow- to a broad-based stance invokes a change in balance strategy from ankle to hip to trunk and in degree of control by stiffness (Day et al., 1993; Winter et al., 1998). Not surprisingly, sway path lengths in both men and women were greater in the anterior–posterior than medial–lateral direction with a broad-based stance, indicative of ankle and plantar control in maintaining stability. The anterior–posterior sway increased with age in the men but not the women, suggesting a reduction in ankle and plantar control in older men. With feet together, however, sway was

exaggerated in the medial–lateral compared with the anterior–posterior direction, indicative of hip control over stability (Winter et al., 1998). Although the gain in stability was greater in the men than women, possibly because the men were slightly less stable in the more challenging conditions than the women, sway in both directions with feet together was greater in older than younger men but not women. These results comport with other studies of community-dwelling adults, showing that women had greater postural control than men in older age (Bryant et al., 2005; Raiva et al., 2004). Although ours was a cross-sectional study, the positive age regression of the present study is indicative of a potential decline in postural control with age, observed longitudinally (cf. Baloh et al., 2003), that is, more profound in men than women.

4.2. Open-loop and closed-loop components of postural stability

Application of the diffusion model of Collins and colleagues (Collins and De Luca, 1993, 1995b; Collins et al., 1995) for examination of the effects of age and sex on components of sway revealed steeper slopes of the short-term, open-loop component with advancing age in men but not women. This model is one of the many proposed to account for the components of balance control and the potential of factors influencing or interacting with control components; others include the spring model (Winter et al., 1998), the inverted pendulum (Balasubramaniam et al., 2000) and its variants (Bortolami et al., 2006), and sway referencing (Peterka and Loughlin, 2004). With no or few sensory aids, the older men exhibited poorer (that is, more unregulated) sway control by the open-loop system but more tightly regulated sway control by the closed-loop system than women. The presence of sensory aids normalized the operation of both control systems in the men and women as well as reducing sway. The characteristics of open-loop and closed-loop control observed in the men is consistent with the initial study of aging using this model (Collins et al., 1995) and extends it by identifying sex differences in open-loop sway control.

One question we posed with our experiment was whether sensory tactile and visual aids could shorten the open-loop component to enhance regulation of balance control. The answer was that a significant sex-by-cue condition interaction in the open versus closed-loop ANOVA indicated different patterns of responses in men and women: the time women took to switch from open- to closed-loop control was shorter in the difficult than easy conditions, whereas the opposite was the case for men. In other words, in situations precarious for balance, women switched to a highly regulated balance control system; men did the opposite. The sex differences can be interpreted as physiologically based differences in strategies to reduce imbalance, where the women used an efficient strategy when challenged with difficult balance conditions, whereas men used an efficient balance strategy only under easy conditions (that is, with sensory aids).

The effect of presence versus absence of sensory and stance aids in the older controls was similar to that observed in a group of alcoholic men, irrespective of age (Sullivan et al., 2006). Here, when no or few cues were available, older controls showed less control over sway during static stance than did younger controls. This age-related instability could be attributed to poor open-loop control. To the extent that measures of static posture are predictive of falling (Shubert et al., 2006; but see Baloh et al., 2003), dwelling in the early, open-loop control system may put individuals at risk for falling by reducing their ability to take advantage of environmental information to enhance stability. Like the alcoholics, older controls were able to take advantage of sensory and stance aids to control sway; however, age did not detectably affect posture regulation by closed-loop control. An hypothesis (Collins et al., 1995; Lauk et al., 1999) posed to explain physiological underpinnings of how environmental cues and feedback work posits that presence of sensory and motor cues reduce musculoskeletal stiffness. Muscle stiffening, which is marked by high open-loop activity when cues are not available, may be a useful strategy for correction of small perturbation to balance, but when excessive,

such stiffening produces inflexibility and becomes difficult to control and may itself induce instability.

4.3. Neuropsychological correlates of postural stability

Studies of postural control in demented populations generally indicate declining stability with advancing dementia (reviewed by Scherder et al., 2007). Whether cognitive status in healthy, nondemented adults exerts an influence on postural control is controversial (Coppin et al., 2006; Rankin et al., 2000; Weeks et al., 2003). In our study, we used the Dementia Rating Scale score as a measure of general cognitive status, and it proved to be a correlate of postural stability in women but not men. Even though no subject scored in or near the range of dementia, lower scores were related to longer sway paths of the women in the conditions with aids, suggesting a role for cognition in using sensory information to improve balance. This possibility is consistent with the shorter time interval between open-loop and closed-loop control, which theoretically can be influenced by cognitive and attentional factors (Collins and De Luca, 1995a), exhibited by the women when cues are available. Thus, higher cognitive abilities may enable women to better use environmental cues. In contrast to the women, men did not show this relation, and neither group showed significant selective correlations between general cognitive status and either open- or closed-loop components of balance regulation.

4.4. Brain correlates of postural stability

Regionally general but not specific measures of brain integrity were predictive of sway path components. Thus, in contrast to MRI findings in individuals with known focal cerebellar compromise that relates to gait and balance impairment (Sullivan et al., 2000, 2006), volumes of the anterior superior vermis were not predictive of balance performance in healthy men or women. Rather, larger volumes of supratentorial CSF and the body of the ventricular system (indices of brain tissue volume reduction) correlated with longer sway paths in men, although the supratentorial CSF measure accounted for the greater proportion of the unique variance of the relation with balance measures without aids. In addition, greater volumes of supratentorial CSF were predictive of steeper slopes of the short-term, open-loop component in the men.

In concert with the cognitive predictor of stability, measures of brain integrity of the women were better predictors of aided than non-aided balance performance. Although the most consistent simple correlations were between volumes of white matter meeting criteria for WMHI and sway path length, ventricular and supratentorial CSF volumes were additional strong predictors – over and above the significant contribution from age – of performance in the most challenging condition (eyes closed/no touch/feet together). The major sex difference again centered on the effect of presence or absence of sensory aids on sway path length: brain metrics were sensitive to variance in the no-aid conditions in the men but to the aid conditions in the women.

Overall, the brain structure–balance function relations observed comported with those of others who had identified that burden of brain white matter signal abnormalities and ventriculomegaly correlated separately and significantly with indices of decline in balance control (Baloh et al., 2003; Guttmann et al., 2000; Masdeu et al., 1989; Starr et al., 2003; Tell et al., 1998). Therefore, these neuroradiological signs of the aging brain are concomitants of age-related degradation of cognitive function (DeCarli et al., 2001; Garde et al., 2000; Gunning-Dixon and Raz, 2000; Raz et al., 2007), processing speed (Nebes et al., 2006; Schmidt et al., 1993; van den Heuvel et al., 2006), and the demonstration herein of postural systems. Disruption of white matter integrity may be a mechanism of prolonged sensory conduction (Wolfson, 2001), which could interfere with integration of sensory motor information for producing an action in time and with accuracy. In support of this possibility is an MR diffusion tensor imaging (DTI) study showing that the extent of gait and balance instability measured in healthy men and women

related to measures of microstructural integrity of widespread regions of brain white matter, indicative of myelin degradation (Sullivan et al., 2001).

5. Conclusions

This study identified a number of physiological, environmental, neuropsychological, neuroradiological, and demographic factors that contribute to different components of balance regulation. Full explication of the interaction of these factors would require rigorous study with several-fold more subjects than examined herein. Nonetheless, the results of this study reveal that aging men and women have diminished postural control, associated with cognitive and brain structural involution, in unstable stance conditions and with diminished sensory input but are capable of stabilizing quiet standing with adequate sensory aids. Rehabilitative efforts provide evidence indicating that elderly who have undergone physical training (Menz et al., 2005, 2006; Nagy et al., 2007) can improve postural control and reduce fear of falling (Delbaere et al., 2006). Our data suggest that such improvement may occur even in the presence of non-specific, age-related brain degradation and cognitive decline.

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Fig. 1.

Examples of sway paths (anterior-posterior and medial-lateral directional average) for one trial performed by a 31-year-old man (top) and a 66-year-old man (bottom). The left panel of sway paths displays performance without any experimental aid, and the right panel shows performance when provided all three experimental aids. Note the exaggerated sway path in the no-aid condition of the older man.

Fig. 2.

Examples of brain regions measured. (a) Ventricular system of a 66-year-old man: yellow tones = frontal ventricles; pink tones = body of the ventricles; green tones = occipital ventricles; turquoise = third ventricle. (b) Supratentorial CSF: sagittal, coronal, and axial views of a late-echo fast spin echo image of a 70-year-old man with CSF as the bright intensity and the supratentorial volume outlined in turquoise. (c) White matter hyperintensities: FLAIR images of a 69-year-old woman with WMHI evident in the periventricular zone. (d) Anterior superior vermis: early echo and late echo of a fast spin echo study of a 72-year-old woman with the vermian region of interest noted by the yellow arrow.

Fig. 3.

Means $\pm$ S.E. sway path lengths for the feet-together and feet-apart conditions with eyes open vs. closed and with and without touch for men and women. Note that the data from the men represent a subset published in Sullivan et al. (2006).

Fig. 4.

Means $\pm$ S.E. directional sway path for the feet-together and feet-apart conditions with eyes open vs. closed and with and without touch for men and women. Note that the data from the men represent a subset published in Sullivan et al. (2006).

Fig. 5. Correlations between each sway path length and age for the men and the women. Note the correlation coefficients in the legend.

Fig. 6. Correlations of the sway-reduction index with age in the men and the women. Note the correlation coefficients in the legend.

Fig. 7.
Greater supratentorial CSF volume correlated with longer sway path lengths in the men.

Fig. 8.
Greater white matter hyperintensity burden (WMHI) correlated with longer sway path lengths in the women.

Fig. 9.
Lower Dementia Rating Scale scores correlated with longer sway path lengths in the women.

Fig. 10.

The grand average of the average squared displacement of pairs of points over time of the 12 younger men (<50 years old) and 16 older men (>50 years old). The top pair of curves displays the grand averages of the younger (gray lines) and older (black lines) for the eyes closed/no touch/feet-together condition; the bottom pair displays the grand averages of each group, which appear overlapping, for the eyes open/touch/feet-apart condition. The fast rising arm of the curves reflects the short-term, open-loop component of the sway diffusion, and the flatter sloped curve reflects the long-term, closed-loop component. The critical point is the intersection between the short-term and long-term slopes.

Table 1Group descriptions of the participating men and women: mean $\pm$ S.D.

	Men ^a (N = 28)	Women (N = 38)	<i>t</i> -Test, <i>p</i> -value
Age (years)	53.2 (12.5)	54.1 (11.7)	n.s.
Education (years)	16.7 (2.0)	16.2 (2.2)	n.s.
Handedness index (right = 14–30; left = 50–70)	18.7 (5.1)	23.0 (16.4)	n.s.
Socioeconomic status	18.8 (8.0)	22.4 (9.3)	n.s.
NART IQ	113.3 (6.5)	113.7 (5.5)	n.s.
WASI Full Scale IQ	117.8 (14.3)	118.5 (10.5)	n.s.
Dementia Rating Scale (max. = 144)	140.3 (3.1)	140.8 (2.4)	n.s.
Mini-Mental Status Exam (max. = 30)	28.3 (1.4)	28.3 (1.4)	n.s.
Body mass index (BMI)	27.4 (4.5)	25.0 (4.3)	.0302
Lifetime alcohol consumption (kg)	72.2 (73.1)	31.2 (32.3)	.0033

^aNote that the data from the men represent a subset published in Sullivan et al. (2006).