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Postural Sway Characteristics Are Affected by Alzheimer's Disease

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Abstract— **The vestibular system, responsible for balance, is affected by Alzheimer's disease (AD). In this paper, linear and non-linear balance features were used to assess the postural stability of 13 AD individuals at mild stages in comparison with 16 healthy controls. Utilizing two accelerometers, the anterior-posterior (AP) and medial-lateral (ML) sways were recorded from the T2 vertebrae and lateral malleolus of participants standing on a solid and soft foam surface under both eyes-open and eyes-closed conditions. From the recorded signals, four features were extracted and used for statistical analysis: Number of Position Changes (NPC), Number of Non-Zero Accelerations (NNZA), Katz, and Higuchi fractal dimensions (KFD and HFD, respectively). The results show: 1) postural stability is significantly worse for the eyes-closed compared to eyes-open condition (P<0.05 for all features except HFD) as well as whilst standing on soft foam compared to the solid surface (P<0.05 for all features) in both groups; 2) balance perturbations were larger for AP sway than ML on both solid and foam surfaces in both groups (P<0.05 for NPC and NNZA); and 3) stationary balance is significantly poorer for AD individuals compared to controls (P<0.05 for all features). These observations show that both linear and non-linear characteristics of postural stability data have the potentials to be used as objective diagnostic aids for the detection of AD.**

I. Introduction

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive memory loss. Presently, AD and other subtypes of dementia affect over 500,000 Canadians, and this number is expected to rise to nearly 1 million by 2031 [1]. Current common cognitive assessment methods used for diagnosis and monitoring any treatment efficacy include verbal fluency tests [2], memory battery tests [3], and questionnaires [4]. However, these assessments can be subjective and dependent on the patient's mood and may lead to a missed or delayed diagnosis, especially in the early stages of the disease [5]. There is a need for objective diagnostic and monitoring measures to identify AD from the cognitive changes that occur due to normal aging. Based on the physiological connection between the balance system's function and the parts of the brain impacted by AD (in particular the brainstem) [6], the balance system's changes (and subsequent decreases in postural stability) may present an opportunity for the identification of new objective measures for assisting early diagnosing of AD from age-matched healthy individuals.

Maintaining postural stability (balance) is achieved through integrating information received from three systems: the vestibular, somatosensory, and visual systems [7]. Several reports are supporting the notion that the vestibular system is impaired in AD, which can result in reduced postural stability. Moreover, there are several vestibular pathways involved in sensory information integration and cognition that run through subcortical nuclei affected by AD, including the thalamus, nucleus accumbens, and hippocampus [8]. Greater atrophy in these areas is associated with poorer postural stability and greater cognitive impairment [9]. This is consistent with several other studies reporting that reductions in postural stability are proportional to the degree of cognitive impairment in AD [10].

Linear (e.g., stride length) and/or non-linear (e.g., fractal dimension) features have been extracted in previous studies to analyze postural stability and gait data from AD aging individuals. However, it has been suggested that fractal dimension analysis is more informative about posture control than linear measures [11]. Unlike linear methods that consider motor variability differences between two groups as a result of random processes (noise), fractal dimension (FD) methods assume that these variabilities may be inherent within the system [12], [13]. Among several fractal dimension methods, Katz and Higuchi's algorithms are two commonly applied methods used in the determination of the FD of one-dimensional biological time series. These methods provide a fast computational tool to determine biosignal variabilities.

In our study, we have utilized both linear and non-linear features to analyze postural sway data. To the best of our knowledge, no previous study has used these features to investigate whether postural sway features are different between AD and age-matched controls and whether these differences vary under different conditions such as eyes-closed versus eyes-open and also foam versus solid surfaces. Also, in this study, a linear regression was used to investigate the association between cognitive test scores (MoCA) and postural stability using the extracted features.

II. Methodology

A. Participants

Two groups of individuals participated in this study: healthy controls and mild to moderate AD patients. All participants read and signed a consent form approved by the Biomedical Research Ethics Board of the University of Manitoba prior to the experiment. AD participants were recruited from our ongoing clinical trial of AD treatment [14], in which all participants have an AD diagnosis confirmed by a

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specialist (a neurologist or a psychiatrist). Healthy controls were recruited mainly from the family members of the AD participants. Participants were assessed by Montreal Cognitive Assessment (MoCA), Vestibular Disorders Activities of Daily Living Scale (VADL), Montgomery-Asberg Depression Rating Scale (MADRS) (control group only), Cornell Scale for Depression in Dementia (CSDD) (AD group), and Clinical Dementia Rating (CDR) (AD group only). None of the participants were clinically depressed. Data of the AD group were collected at baseline before they received the treatment.

The inclusion criteria identifying the healthy controls were as follows: 1) having 55 years of age or older, 2) able to communicate in English, 3) have a MoCA score ≥24, and 4) attaining a MADRS score ≤19. The inclusion criteria for the AD participants are presented in [23] in detail; in relation to this study they had: 1) age of 55 years or more, 2) a MoCA score between 7 to 25; 3) a CDR score of 1 to 2, and 4) a CSDD score of ≤18. For both groups, individuals with psychiatric conditions/disorders (e.g. schizophrenia, bipolar affective disorder, severe agitation, prominent anxiety), neurological/systemic/medical disorders, mental retardation, impaired visual and auditory confounding performance in cognitive tests were excluded from the study. Table 1 shows the demographics of both groups. The values show mean±STD where applicable. The experiments were conducted at Riverview Health Center, Winnipeg, Canada.

TABLE I. PARTICIPANTS DEMOGRAPHICS.

Characteristics	Controls (n=16)	AD (13)
Female/Male	12/4	5/8
Age	65.37±10.23	72.53±6.85
MoCA	26.56±2.44	14.07±5.20
MADRS	2.93±2.54	-
CSDD	-	1.92±2.98
CDR	-	1.07±0.27
VADLs	1.09±0.19	1.17±0.21
Wight (kg)	75.63±11.61	71.13±13.62

B. Postural Sway Experiment

Postural sway was measured using a custom-designed device for measuring the balance sway in two anatomical planes (sagittal and coronal) by placing two 3D accelerometers (Adafruit BNO055 board) on the T2 vertebrae and ankle (lateral malleolus) as suggested in [15] using Velcro bands (Fig. 1). Data were recorded with a 100 Hz sampling rate. Each accelerometer was calibrated before attachment to the participants to ensure reliable data recording. Next, the sensors were attached and measurements were taken while standard balance tests were performed on a solid surface (floor), and then on a 50.8 cm x 50.8 cm x 10.16 cm (L x W x H) memory foam sponge. For both surfaces, participants stood with feet shoulder-width apart and arms crossed over the chest while data were collected for a duration of 30 seconds with eyes-open gazing at an eye-level wall-mounted marker, and for another 30 seconds with eyes-closed (when vestibular and somatosensory inputs play a larger role in postural stability maintenance). At all times, two research assistants were present on either side of the participant to provide physical support in case participants begin to lose their balance. Data of each participant included movement in three directions (x, y, and z axes). The signals in AP and ML planes were analyzed.

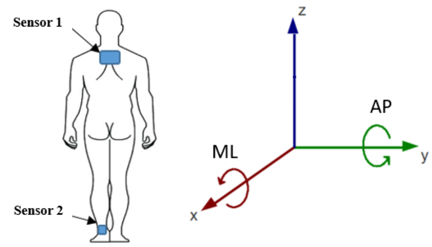

Figure 1. Sensor placement and sway directions. Sensor 1 and 2 were located on the T2 vertebrae and ankle respectively.

III. DATA ANALYSIS

Linear and non-linear features of the recorded signals in each of the AP and ML directions were extracted. The linear feature was: number of position changes (NPC); the non-linear features were: number of non-zero accelerations (NNZA), KFD, and HFD. The NPC was calculated by taking the difference between two consecutive samples. If this difference was non-zero (meaning that the position of the individual has changed from the previous position), the NPC increased by one. Similarly, the NNZA was calculated for each two consecutive data points. The NNZA (indicative of moving/accelerating from a stationary standing position) over 30 seconds of recording was determined as our second feature.

Equations 1 and 2 show the Katz and Higuchi algorithms used in this study.

$$KFD = \frac{\log(n)}{\log(n)+\log\frac{d}{L}},\ d = max\{y_k\} - min\{y_k\},\ L = \sum_{k=1}^{n} |y_{k+1} - y_k| \quad (1)$$

$$HFD = \frac{\log(L(K))}{\log(1/K)} \quad \text{Slope of least squares linear best fit} \quad (2)$$

Where $L(K)$ is the average curve length calculated for k sets of $L_m(K)$, m indicates the initial time, and K denotes the interval time which goes from 1 to K_{max} . The parameter K_{max} in Higuchi equation was obtained according to [16], and considered to be equal to 500. For each participant, these features were extracted for a total of sixteen different combinations of accelerometer position (T2 vertebrae and ankle), directions of sway (AP and ML), and experimental conditions (eyes-open, eyes-closed, solid, and foam surfaces).

A factorial repeated measure ANOVA was conducted to investigate the within-subject effect of the experimental conditions in control and AD groups. To identify whether the extracted features of postural sway are correlated with cognitive impairment in early and moderate Alzheimer's disease, we performed a linear regression (back elimination method) between the MoCA score with postural sway in different conditions on the foam surface (standing support was the only condition that resulted in a significant difference for all the features).

A mixed model analysis of variance (Mixed ANOVA) was conducted in SPSS to investigate whether healthy control and AD individuals showed any significant difference in terms of postural sway features. The significance level was considered less than 0.05 in all instances. Bonferroni method was used for confidence interval adjustment.

IV. RESULTS

Demographic participant information was compared using an independent sample t-test, which showed a significant difference ($P<0.001$) between the MoCA scores of healthy controls and that of AD individuals as expected. However, the VADL scores showed no significant difference. The obtained results for each feature are presented in the following sub-sections.

Figure 2a-d shows the results of the extracted feature. In both healthy controls and AD groups, the number of changes in the position was significantly higher for the eyes-closed versus eyes-open condition ($P\leq0.042$ for NPC, NNZA, and KFD), foam surface versus solid surface ($P\leq0.001$ for all features) as well as AP sway versus ML sway ($P\leq0.001$ for NPC and NNZ).

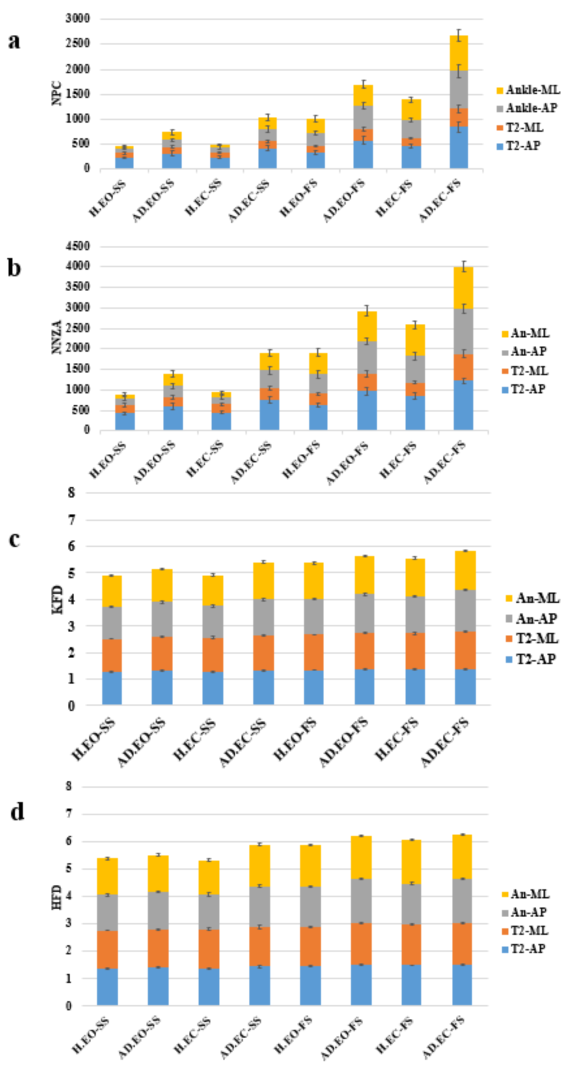

Figure 2. Comparison between healthy controls and AD patients using the linear and non-linear features. Values are shown as (Mean±SE); The average NPC (Fig. 2a), NNZA (Fig. 2b), KFD (Fig. 2c), and HFD (Fig. 2d) are significantly higher for AD patients compared to the control group. Legends: T2 and Ankle represent the accelerometers' position, AP and ML represent anterior-posterior and medial-lateral sways, respectively. H: Healthy; EO: Eyes Open; EC: Eyes Closed; SS: Solid Surface; FS: Foam Surface.

Performing a linear regression (backward elimination) to investigate the correlation between the balance data recorded on the foam surface with MoCA scores of AD individuals, a significant regression equation was found only for NNZA (($F(7,12)=5.98$, $P=0.033$), $R^2=0.893$ considering the MoCA score as the dependent variable and all independent variables except AP data recorded from the T2 sensor with eyes open as predictors) and Katz (($F(1,11)=5.39$, $P=0.040$), $R^2=0.329$ considering the MoCA score as the dependent variable and the ML sway data recorded from the ankle with eyes closed as the predictor) features. The between-subject effects test showed a significant difference between healthy and AD individuals for all features ($P\leq0.033$, power≥0.583, $\eta^2\geq0.154$).

Considering the two-way interactions with the groups, AD individuals showed poorer postural stability for different experimental conditions including foam or solid surface ($P=0.018$, power=0.677, $\eta^2=0.189$ only for NPC), eyes open or closed condition ($P\leq0.015$, power≥0.710, $\eta^2\geq0.201$ for NPC and NNZA), and direction of sway ($P=0.016$, power=0.696, $\eta^2=0.196$ only for NPC). The interaction of groups and sensor positions (T2 vs ankle) did not lead to a significant difference ($P=0.499$, power=0.101, $\eta^2=0.017$) for any of the four features.

V. DISCUSSION

In this study, linear and non-linear postural stability features of healthy older adults and individuals with mild and moderate AD were investigated. In general, the AD patients showed poorer balance stability compared to the healthy older adults under different experimental conditions for all features. Furthermore, a significant correlation ($P<0.04$, $R>0.574$) was found between the severity of impairment (MoCA score) and the postural stability features (NNZA, KFD). These results become more important when considering that the VADL questionnaire showed no difference among the groups. This indicates AD group may not have any apparent balance disturbances, while their postural stability is still impacted by the disease, and such impact can be detected by postural sway analysis.

Research on the aging population has provided strong evidence for reduced postural stability of mild and moderate AD individuals in comparison with healthy older adults [10]–[12], [17]. In [18], linear features including the center of pressure, path length (mm), and mean velocity (mm/s) were used to analyze the postural stability data of older adults with cognitive impairment recorded on a force plate. Difficulty in movement planning, increased sway, and higher risks of falls (two times higher than older adults without cognitive impairment) were reported for individuals with cognitive impairment compared to the control group. Doyle (2004) used linear (range of sway) and non-linear (Higuchi's fractal dimension algorithm) methods to discriminate between healthy young and elderly individuals [11]. The authors concluded that the FD analysis could be more informative about postural control than traditional measures as it could be an indicator of pathology due to aging. Using Rényi fractal dimension, the study in [13] revealed a significant difference between young healthy individuals and elderly patients with balance impairment and a history of frequent falls. Higher values of FD were associated with the patient group and increased difficulty of the task by eliminating visual inputs and or by adding somatosensory perturbation. Our study's results, although in a separate population, are congruent with the above findings. The four postural stability features used in this study showed potential in discriminating healthy elderly individuals from their age-matched Alzheimer's group. However, the NPC was a better differentiator in terms of the within-group and between-group effects, and the NNZA and KFD had higher correlations with the MoCA scores.

It has been shown in [19] that decreased/ absence of visual inputs or incongruent visual, vestibular, and somatosensory information contributes to the postural instability of AD subjects. These observations are not unexpected given the distributed network between these sensory systems that includes several common subcortical (superior colliculus, thalamus, hippocampus), cortical (insular cortex), and cerebellar (vestibulocerebellum) brain regions that integrate visual, vestibular, and somatosensory information [20]. Moreover, the increased motor variability for the aging people compared to young individuals, and mild to moderate AD compared to the healthy older adults have been reported in [11], [12]. It has been stated in [17] that increased motor variability of elderly individuals due to decreased motor control can be developed in AD individuals to reduce risks of falls. Our findings from the presented study are in agreement with the mentioned studies showing a reduced postural balance in the absence of visual inputs (significant for the NPC and NNZA features) in both groups as well as an association/correlation between postural sway and the cognitive impairment (significant for the NNZA and KFD).

The presented study shows the potential use of postural sway features for objectively assessing AD patients; these features may also be very useful to identify subtle changes after treatments while questionnaire measures such as VADL fail to detect them.

VI. Limitations

The main limitation of this study is the small sample size of participants, which was mainly due to the COVID-19 lockdown that the study has been on hold since March of 2020.

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