2017 CMBEC40 Conference
Winnipeg MB
May 23–26, 2017

# EVESTG DIAGNOSTIC POTENTIALS FOR NEURODEGENERATIVE DISORDERS

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## INTRODUCTION

Electrovestibulography (EVestG) is a non-invasive diagnostic technology that measures the electrical activity of vestibular system including vestibular hair cells, vestibular nerve and vestibular nucleus (VN), as well as several brain regions which broadly communicate with the VN in the pathophysiology of neurological disorders [1, 2]. EVestG technique is similar to Electrocochleography (ECOG) [3], wherein the acoustic stimulus are replaced by a passive whole body tilt. During the experiment, ear canal electrical activities are recorded in response to dynamic and static phases of a computer-controlled hydraulic chair via an electrode resting painlessly proximal to the tympanic membrane. Fig. 1 shows the recording system with the hydraulic chair.

Studies have shown that EVestG signal analysis can provide unique biomarkers for individuals with Meniere's disease, Major Depression disorder and Parkinson's disease [1, 4, 5]. Early stage investigations have also shown diagnostic potential of EVestG signal analysis for Post Concussion Syndrome (PCS) and Dementia [6, 7].

Characteristic features specific to a disorder can be derived from the EVestG signal during the static or dynamic phase of the experiment. Herein, we use only the static phase features derived from the spontaneous activity of vestibular hair cells in the absence of any vestibular stimulation. We hypothesize that statically-derived EVestG signal features can be used to discriminate a healthy versus neurodegenerative pathological functioning of the vestibular system and the connected brain regions. If such information exists, we can then use it as a biomarker for a simple screening tool to detect individuals as healthy or with neurodegenerative pathology during a first stage screening examination.

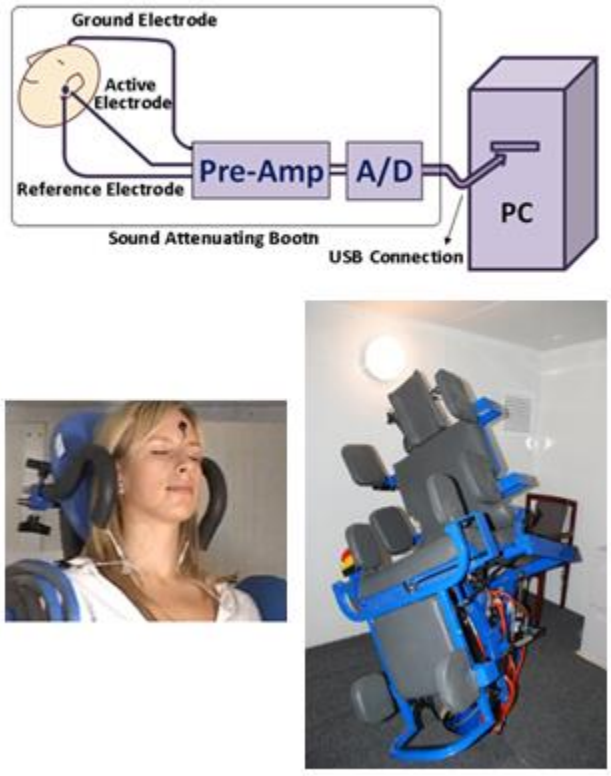


Figure 1: EVestG recording system with Hydraulic chair.

In this pilot study, we analyzed EVestG signals of three groups of individuals suffering from neurological disorders including 10 individuals diagnosed with Dementia, 20 with

Parkinson's, and 35 with PCS in comparison with EVestG signals of 64 healthy controls.

## METHODOLOGY

### *A. Data*

Our data came from two identical EVestG laboratories at: 1- The Alfred Hospital, Melbourne, Australia, and 2- Riverview Health Center (RHC) in Winnipeg, Canada. Data of three neurodegenerative disorders, Parkinson's, PCS and Dementia, were adopted from our other studies. Ethics approval was granted by the Biomedical Research Ethics Board of the University of Manitoba and Alfred Hospital; all study participants signed an informed consent form prior to the experiments.

Parkinson's data were from 20 individuals ($65.8 \pm 6.8$ yrs, 10 males), who were recorded while they had been off their medication (Levadopa preparations) for at least 4 hours and typically overnight [1]. The severity of the Parkinson's was assessed using the Modified Hoehn and Yahr PD Staging Scale [12]. Using this scale, out of the 20 Parkinson's individuals, one was severely affected while the others were at mild to moderate stages.

PCS data included EVestG signals of 35 individuals ($42.9 \pm 13.7$ yrs, 17 males) with PCS. The duration between brain injury and the recording date was between 2 weeks-19 years. The PCS participants were examined, completed comprehensive neuropsychological assessments, and diagnosed by the team's neurologist [7].

The dementia data included EVestG signals of 10 individuals ($76.7 \pm 7.4$ yrs, 5 males) diagnosed with Dementia [6]. The Dementia participants were verified using questionnaires and assessment by a psychiatrist.

In addition to the above data sets, we used EVestG signals of 64 healthy individuals (51.9±9.4, 32 males) as the control group.

### *B. EVestG Experiment*

In a typical EVestG experiment the participant sits in a hydraulic chair with eyes closed and head rested on the chair headrest, while the electrodes already attached to him/her and to the chair. The hydraulic chair is placed inside a dark acoustically attenuated (>30 dB) and electromagnetically shielded chamber.

The time segment analyzed herein corresponds to the 1.5sec prior to any applied tilt (stimulus). It is labelled BGi. There were 5 segments of 1.5sec each that were recorded for each participant. All five BGi segments were included in the analysis. EVestG signals were recorded at a sampling rate of 41666 Hz.

### *C. Signal analysis*

After the recordings, ear signals along with the background noise were fed to the NEER algorithm [3] to extract two main signals: average field potential (FP) and its firing pattern from the BGi segments for each ear. We averaged the FP curves of the five BGI segments of each individual, and normalized the average FP curves by their absolute value of the action potential (AP) point (shown in Fig. 2). Then, we calculated the AP region (the area above the AP point and under the baseline shown in Fig.2) as a characteristic feature. Then, we used the one-tailed *t*-test to investigate whether this feature was significantly different between the two groups of healthy controls and those with one of the three neurological disorders. This analysis was done for each ear's signal separately.

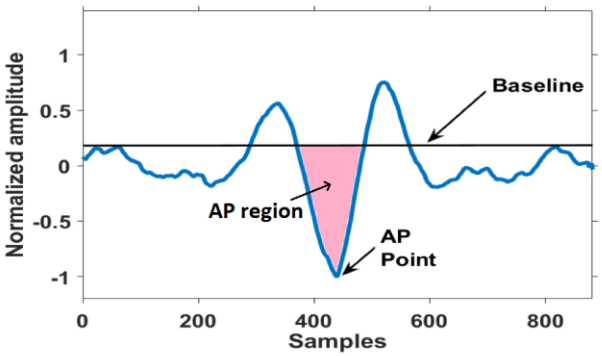


Figure 2: A typical normalized FP extracted from a control participant during a BGI phase.

## RESULTS

Figures 3 and 4 show the mean and 95% interval of the FP curves of healthy controls versus those of the neurological group. There were three areas of separation for all three neurodegenerative disorders on both the right and left ear signals between the two groups. In this pilot study, we only selected one feature

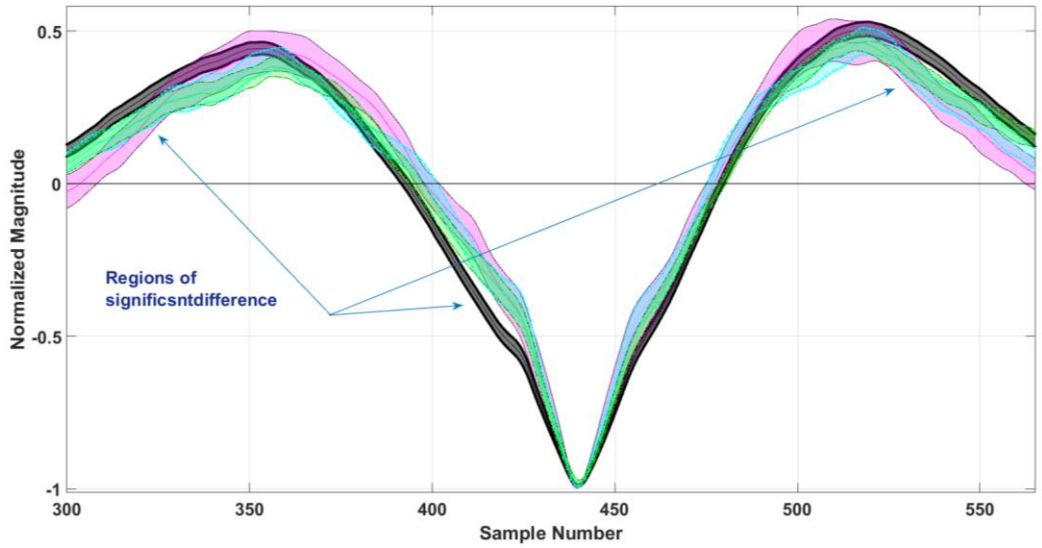


Figure 3: 95% confidence regions for the right side average signal of control FPs versus the average signal of FPs for Control, Dementia, PD and PCS pathologies, respectively. Plots have been dilated along the horizontal axis to provide a clearer picture of significant control versus Neurodegenerative disorder different regions.

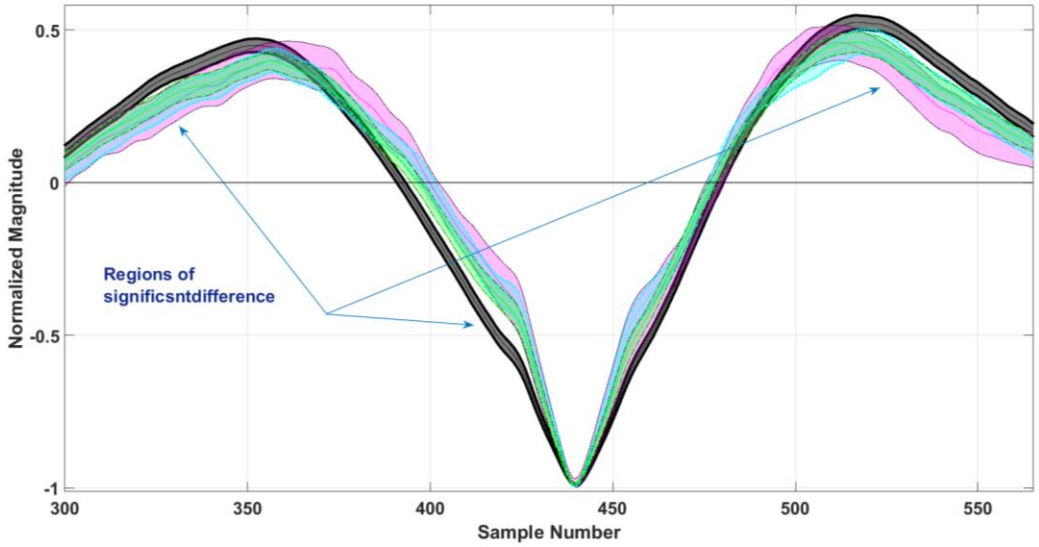


Figure 4: 95% confidence regions for the left side average signal of control FPs versus the average signal of FPs for Control, Dementia, PD and PCS pathologies, respectively. Plots have been dilated along the horizontal axis to provide a clearer picture of significant control versus Neurodegenerative disorder different regions.

(the AP-area) to investigate there are statistically significant differences between the two groups. Mean and standard deviation of the AP-area feature for the left ear signals were 34.8±9.8 and 43.3±9.6, for neurological and control groups, respectively. The values for the right ear signals were 34.8±9.7 and 41.5±8.3 for neurological and control groups, respectively. A t-test showed significant differences ($p<0.001$) between the two groups for both ear signals.

## DISCUSSION

The hypothesis was that statically-derived EVestG signal features can be used to discriminate normal versus neurodegenerative pathology. Just looking at the 3 common regions on the left and or right side it is clear that discrimination can be made and that that discrimination is significant for the AP region feature. In a future analysis, the use of the minimum area of the left and right sides might allow for sidedness issues particularly apparent in PCS to be better accounted for. Literature abounds on the impact of neurodegenerative disorders on the balance system but there has been little focus on their impact at a peripheral vestibular system level.

In PD the evidence for physical and metabolic change in vestibular pathway nuclei within descending projections at least to the VN is established. Indeed we argue in [1] that dopamine levels can also impact the vestibular periphery. The presence of 'sensitive' dopamine (and other) receptor processes potentially capable of regulating membrane excitabilities through response neurochemistry utilizing processes that may involve co-activation and/or alteration of ionic processes and which are often targets of PD drugs is supportive of some peripheral impact.

Dementia and PCS/mTBI have some similarities in that there are suggestions/evidences of axonal mechanisms such as ion channel numbers are effected post-concussion or during Dementia, each potentially being the result of beta amyloid or related protein build ups in axons [8, 9].

Future research needs to look at reanalyzing these data groups with larger sample sizes and age matching. Additionally, a search for overlapping physiological changes in each of the pathologies that have an association with the common significant different regions of the field potential may provide understanding of the common changes observed.

## References


[1] B. J. Lithgow and M. Shoushtarian, "Parkinson's Disease: Disturbed vestibular function and Levodopa," *J. Neurol. Sci.,* vol. 353, pp. 49-58, 2015.

[2] C. Gurvich, J. J. Maller, B. Lithgow, S. Haghgooie, and J. Kulkarni, "Vestibular insights into cognition and psychiatry," *Brain Res.,* vol. 1537, pp. 244–259, 2013.

[3] B. J. Lithgow, "A methodology for detecting field potentials from the external ear canal: NEER and EVestG," *Ann. BME* vol. 40, pp. 1835-1850, 2012.

[4] B. J. Lithgow, A. L. Garrett, Z. M. Moussavi, C. Gurvich, J. Kulkarni, J. J. Maller*, et al.*, "Major Depression and Electrovestibulography," *World Journal of Biological Psychiatry,* vol. 16, pp. 334-50, 2015.

[5] Z. A. Dastghieb, B. J. Lithgow, B. Blakley, and Z. Moussavi, "Application of vestibular spontaneous response as a diagnostic aid for Meniere's disease," *Ann. BME,* 2015.

[6] B. J. Lithgow and Z. Moussavi, "Dementia and EVestG," *Asian Journal of Psychiatry,* vol. 4 (supplement 1), p. 56, 2011.

[7] A. Suleiman, B. Lithgow, B. Mansouri, and Z. Moussavi, "Investigating the feasibility of using EVestG assessments for monitoring side (lateral) -impact concussion. ," presented at the 2017 CMBEC40 Conference, Winnipeg Canada, 2017.

[8] N. Arispe, E. Rojas, and H. B. Pollard, "Alzheimer disease amyloid β protein forms calcium channels in bilayer membranes: Blockade by tromethamine and aluminum (cation channel/phospholipid bilayer)." *Proc. Nati. Acad. Sci. USA,* vol. 90, pp. 567-571, 1993.

[9] X. Chen, R. Siman, A. Iwata, D. M. Meaney, J. Q. Trojanowski, and D. H. Smith, "Long-Term Accumulation of Amyloid-β, β-Secretase, Presenilin-1, and Caspase-3 in Damaged Axons Following Brain Trauma.," *Am. J. Pathol.,* vol. 165, 2004.