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USING POSTUROGRAPHY IN A PRACTICE-BASED SETTING TO INVESTIGATE THE EFFECT OF SACCADES IN HEALTHY SUBJECTS

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ABSTRACT

Eye movements such as saccades are utilized in therapeutic strategies in clinical settings within psychiatry, psychology, vestibular therapy, occupational therapy, physical therapy and chiropractic. Attempts have been made to measure the relationship between saccades and postural stability within laboratory conditions. Conflicting information exists as to whether healthy subjects have decreased or increased postural stability during saccades compared to unhealthy subjects. Few practice-based saccade/postural stability study designs have been developed to gather normative data from healthy subjects. In this study, a robust, portable clinical study design that could statistically withstand variability across a range of practice-based clinical settings (including location and tester) was developed allowing changes in subject postural stability data to be grouped and analyzed over those settings. This is the first step for using such a design within a Practice-Based Research Network (PBRN) Randomized Clinical Trial (RCT) methodology to assess the outcomes of saccade-based therapeutic strategies on postural stability in non-healthy cohorts. The results of this investigation show that it is possible to develop a robust clinical design to test the effect of saccades on postural stability that can be used across a range of practice-based settings. The impact of the instrument portability, robustness and sensitivity, of the pre-study tester training (adhering to data retrieval methodology and subject recruitment criteria), and of the environmental variability within location settings should not be under-estimated when designing a practice-based clinical study to guarantee data reliability and validity.

Keywords: Practice-Based Research Network, Randomized Clinical Trial, balance, posturography, saccades, clinical protocol, study design

INTRODUCTION

Eye movements and postural stability are integral components of the efficient, adaptive human bipedal balance system. Strong neural network connections exist between neural centers driving saccades (a type of eye movement) and those centers maintaining postural stability [1]. This allows humans to remain upright and maintain optimum whole body motor function over a wide range of varying visual and postural conditions. Damage to, or developmental delay of neural connections between centers of oculo-motor activity and postural stability has been found to have a negative impact on human balance and function [2]. Furthermore, the health and economic consequences of balance dysfunction has driven research interest in saccade-postural stability interaction, particularly in the area of falls risk [3].

Published computerized posturography (CP) research investigating saccade-postural stability interaction has identified the effect of saccades on postural stability over a range of sensory and motor conditions within healthy and unhealthy cohorts. For instance, CP analysis has been used to explore how differing subject characteristics (e.g., age and gender) and saccade performance conditions (e.g., varying directions, pace and salience of saccade search) impact saccade-postural stability interaction amongst healthy subjects [4, 5]. Typically, such saccadic-postural stability studies are laboratory-based within a tertiary research or clinical setting and use methodologies that assess small-size cohorts from a single data collection setting of convenience (often enrolled university students) under laboratory conditions that significantly control for experimental "noise" [6]. The outcomes from studies with these methodologies have been developed from these experimental settings to investigate therapeutic strategies that include saccade and postural stability training [7]. However, clinical saccadic performance-postural stability assessment and therapeutic training are mostly performed in smaller primary and secondary health and home-care settings under low-tech clinical assessment conditions with significant assessment "noise" [8]. Practice-Based Research Networks (PBRNs) provide the opportunity to analyze data from a broader collection base more representative of the therapeutic assessment or intervention setting [9]. PBRN methodologies have been developed over the past decade to improve the collection of research data over a range of clinical settings [10]. There are many challenges and considerations when designing and implementing practice-based clinical research within the areas of saccadic performance and therapeutic intervention strategies when using postural stability as a clinical outcome measure. Using a mobile force platform as a testing instrument, we have designed a robust, portable clinical study that should withstand variability across a range of practice-based clinical settings. This study was developed to allow changes in a healthy subject's individual postural stability data following perturbation by saccades to be detected, grouped and analyzed outside of the traditional laboratory. This investigation represents a pilot study for using such a design within a PBRN Randomized Clinical Trial (RCT).

METHODS

The study was conducted in two separate settings: a *conference setting* and a *clinical setting*. The *conference setting* consisted of multiple testing stations in a large, open-air conference room subject to the environmental stimuli intrinsic to that environment. The *clinical setting* was performed in a dedicated room with a consistent environment and quiet ambiance.

Two groups of 25 individuals participated in this study, approved by our institutional IRB (Registration # 20160321002). Table 1 contains the demographic information for the groups. All participants completed a health questionnaire to identify any comorbidities related to neurological, respiratory, cardiovascular, oncological, balance, auditory, visual, and musculoskeletal conditions; and if they were taking any medications related to these or any other conditions. They were also asked if they had sustained any head or neck injury in the last two years. Each subject underwent an initial posturography testing to independently evaluate their balance, but the results of this testing did not constitute an inclusion/exclusion criterion.

The actual testing protocol consisted of posturographic testing while performing four different 60 s saccade-to-target montages, repeated on a hard surface (*normal stability*) and on a compliant surface (*perturbed stability*): (1) at a *fixed* amplitude and frequency in the *horizontal* plane; (2) at a *random* amplitude and frequency in the *horizontal* plane; (3) at a *fixed* amplitude and frequency in the *vertical* plane; (4) at a *random* amplitude and frequency in the *vertical* plane. Prior to each of the eight trials a 60 s baseline test was performed with fixation on a stationary visual target in central vision. The stimulus montage was displayed on a computer monitor placed on an adjustable stand to compensate for the differences in height between the subjects, as well as between the hard and compliant surfaces, so to guarantee that the stimulus was centered in the subject's visual field. The monitor distance from the subject was adjusted to be sure that the maximal excursion of the eyes was 30°. The eye movements were not recorded nor measured, but observed, either directly or using a video camera mounted on the stimulus computer to ensure that the subject was indeed performing saccades as instructed. Force platforms satisfying the metrological standards set by the International Society for Posture and Gait Research (ISPGR) [11] (CAPS® Lite or Professional with the CAPS® EQ software– Vestibular Technologies, LLC, Cheyenne WY, US) were used to collect and analyze all the posturography data. Acquisition frequency was set at 64 Hz and data were up-sampled to 1 kHz before analysis (more details of data acquisition are available upon request). Each acquisition lasted 65 s, with 5 s pre-test during which the subject looked at a fixed target, and 60 s test during which the subject maintained the upright stance while following the target with eyes only (no movement of head or torso).

The two *horizontal fixed* and *random* montages were created using Mac Keynote software version 6.6.2 on a Macbook computer. The target was an orange (24 bit RGB color 238, 170, 0 - hex: EEAA00) circle with a diameter of 44 pt (equal to a viewing angle of 0.6875°), no outline or shadow, on a solid black background. The initial position for both montages was the center of the screen, which was held for the entire duration of the pre-test. Then, for the *fixed* montage, the target alternatively appeared at the right and left edge of the screen, in midline vertical position without clipping, and held such position for exactly one second. No time gaps were present between targets (the next one appeared when the previous one disappeared). To construct the *random* montage, the same background, target shape, size and color were utilized. The horizontal location on the screen was randomly selected, the only constraints being that two subsequent targets had to be separated by at least 5 degrees so to elicit actual saccades in the subject, and half were right saccades and half were left saccades. The vertical location was held along the vertical midline of the screen. The time between two subsequent targets was a random number between 0.70 s and 1.30 s, with an average of 1 Hz. A total of 64 targets were used in the montages to guarantee that the stimuli lasted the entire duration of the posturographic acquisition. A recording of the montage was generated, then exported as an MPEG-4 file at 1080p resolution. The two *vertical fixed* and *random* montages were obtained by rotating the display monitor 90°, ensuring a vertical maximal saccade excursion of 30°.

The tests were performed in a randomized sequence in regard to stability and saccade stimulus. For each subject the horizontal montages were first completed, then the vertical. In the *conference setting*, the subjects were split into four groups and each subject in the group performed one montage before the

whole group proceeded to the next testing station, therefore each subject had at least 15 minutes of rest between tests. Furthermore, for convenience, the *horizontal* montages were done in the morning and the *vertical* ones in the afternoon of the same day. In the *clinical setting*, each subject was tested individually and sequentially (so there was no appreciable rest time between test montages), and randomly during the day. In both settings, testing personnel included an operator tasked with running the data acquisition, starting the stimulus montage, and adjusting the setup of the stimulus monitor to the appropriate height for each subject; and one spotter positioned near the subject in case of loss of balance.

All the data analysis was performed using IBM SPSS software (SPSS Version 20.0, IBM Corporation, Armonk, NY, US) and consisted of General Linear Model (GLM) multivariate analyses of the demographics and posturography data (to determine if the two groups of subjects were equivalent), and of GLM multivariate analyses and with repeated measures (RM) of the baseline and saccades data (to determine if there was any effect due to the two different groups/locations). Of all the available posturographic data, only the maximum anterior-posterior sway, the maximum medio-lateral sway, the 95% confidence maximum sway, the average velocity, and the 95% confidence ellipse area were considered in the analyses. They were normalized by the height of the subject to allow inter-subjects comparison (the ellipse area was normalized by the square of the subject's height).

RESULTS

Subject groups represented appropriate adult age, height, weight and BMI ranges, with no statistically significant between-group differences ($p = 0.516$, partial $\eta^2 = 0.068$ and observed power = 0.242 for the demographics, and $p=0.272$, partial $\eta^2 = 0.467$ observed power = 0.661 for the results of the posturographic testing). All subjects were self-assessed as being in good health according to responses on the health questionnaire. Table 2 contains the results of the GLM analyses on the baseline and saccades data.

DISCUSSION

The aim of this study was to determine whether a robust, very sensitive and accurate mobile force platform, previously used in laboratory-based computerized posturography studies, combined with a practice-based study design, could account for experimental noise over two significantly different data collection settings and conditions allowing postural stability data to be pooled over the two sites.

Analysis revealed no statistical difference between the data collected from the two sites (Table 2 – GLM-Multivariate and GLM-RM between subjects location). Our study methodology and choice of testing instrument were designed for use in a PBRN. Data collection methods were systematically recorded by each tester and demonstrated high consistency throughout each setting. Our collection sites contained significantly different environments. The *conference setting* provided more opportunity for subject distraction as well as operator and observer variability. Participants inexperienced in CP data collection protocols underwent considerable pre-testing CP education and training, and strictly adhered to data collection protocols. The *clinical setting* consisted of a quieter, less distracting environment, with

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two experienced CP clinicians conducting the study protocol. The fact that our analyses revealed that there were no significant differences between such different collection sites indicates that with adequate education and training, "operator effect" can be controlled for across different testing sites. This should provide confidence to researchers and clinicians to use CP methodologies and subject recruitment strategies when considering intervention studies across multiple testing settings within a PBRN.

Table 1 - Demographics

	Group 1	Group 2	All
# of subjects	25	25	50
Males	11	13	24
Females	14	12	26
Age [years]			
Ave	32.96	38.48	35.72
StDev	13.82	10.32	12.39
Height [m]			
Ave	1.75	1.72	1.74
StDev	0.10	0.09	0.10
Weight [kg]			
Ave	74.82	74.23	74.52
StDev	13.16	18.86	16.10
BMI [kg/m^2]			
Ave	24.29	24.83	24.56
StDev	2.63	5.21	4.09

Table 2 – General linear model results.

Test	Analysis	Test condition	p	Partial η^2	Power
Baselines	GLM-Multivariate	All baselines	0.057	1.000	0.618
	GLM - RM between subjects location	All baselines	0.123	0.177	0.574
		Normal stability	0.212	0.148	0.473
		Perturbed stability	0.083	0.193	0.640
	GLM - RM within subjects repetitions	All baselines	0.018	0.996	0.911
		Normal stability	0.000	0.912	1.000
		Perturbed stability	0.000	0.934	1.000
Saccades	GLM - RM between subjects location	All tests	0.000	0.439	1.000
		Normal stability	0.089	0.193	0.628
		Perturbed stability	0.000	0.461	0.998
	GLM - RM within subjects repetitions	All tests	0.000	0.987	1.000
		Normal stability	0.261	0.370	0.636
		Perturbed stability	0.000	0.782	1.000

Subject data were collected at different times in the two settings. This was designed to mimic a typical practice-based collection setting. Our analysis revealed that this had no statistically significant impact on the results gathered. The *conference setting* subjects were assessed under random allocation grouping across two distinct time periods and allowing significant rest periods between testing protocols. The *clinical setting* subjects were sequentially tested under random allocation over a continuous period with no substantial breaks, which is more similar to the controlled laboratory environment described in the majority of CP studies. This should provide encouragement to practitioners wishing to enroll their busy clinic setting into a PBRN. Individual statistically significant differences were detected for the baselines (Table 2 - GLM – RM within subjects repetitions). Perturbation strategies such as saccades, pursuits and head movements are commonly used within laboratory-based intervention strategies measured by CP outcomes across a range of therapeutic domains. Horizontal and vertical saccades were chosen as the perturbation activity in this study as healthy subjects use saccades in their everyday activities of daily living as well as ensuring the ease of subject training and repeatability required in a practice-based setting. It is important to note that this was not an intervention study; subjects were deemed to be healthy. By design, the study did not include the added complexity of measuring saccades using sophisticated, poorly portable oculomotor recording equipment and software; only the ability of a subject to perform saccades during the postural stability recording period without head movement was considered and observed.

Further analysis of the results revealed that healthy subjects do have individual responses to relatively benign saccadic challenges especially in *perturbed stability* conditions (Table 2 - Saccades). Such individual responses are often ignored in the results of CP studies. The inclusion of repeated baseline measures within the methodology went some way to account for the differing responses to any form of perturbation amongst our healthy subjects and should be included in future studies using CP protocols, as better outcome measures might be relative responses from baseline rather than absolute values.

CONCLUSIONS

Seldom can laboratory conditions be achieved in a clinical environment. Furthermore, the same clinical environment can significantly vary from one location to another. Therefore, it is important to control for environmental variables. When this is not feasible, ensuring a practice-based methodology designed around a robust testing instrument is paramount. This study proposed a practice-based methodology using a protocol that might be considered in future intervention studies using computerized posturography within a PBRN. The study highlighted issues considered in a PBRN including subject variability, testing site differences, data collection times, operator training and healthy subject responses to perturbation across significantly different data collection sites that might represent differences faced in a PBRN. Our results revealed that data collected using force platforms that meet the ISPGR standards would seem to be robust in field-data collection. Therefore, clinical studies may be run in non-laboratory settings and data from multiple sites can be pooled, allowing changes in subject's postural stability data to be grouped and analyzed over those settings. Our results recommend a methodology and testing instrument that can be considered for use in PBRN saccade intervention designs across multiple clinic settings and should provide an impetus for further PBRN designs.

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