The Effects of Visual Context on Visual-Vestibular Mismatch Revealed by Electrodermal and Postural Response Measures

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Abstract

BACKGROUND

No objective criteria exist for diagnosis and treatment of visual-vestibular mismatch (VVM).

OBJECTIVE

To determine whether measures of electrodermal activity (EDA) and trunk acceleration will identify VVM when exposed to visual-vestibular conflict.

METHODS

A modified VVM questionnaire identified the presence of VVM (+ VVM) in 13 of 23 young adults (34 ± 8 years old) diagnosed with vestibular migraine. Rod and frame tests and outcome measures for dizziness and mobility were administered. Participants stood on foam while viewing two immersive virtual environments. Trunk acceleration in three planes and electrodermal activity (EDA) were assessed with wearable sensors. Linear mixed effect (LME) models were used to examine magnitude and smoothness of trunk acceleration and tonic and phasic EDA. Welch's t-test and associations between measures were assessed with a Pearson Correlation Coefficient. Effect sizes of group mean differences were calculated using Cohen's d test.

RESULTS

Greater than 80% of all participants were visually dependent. Outcome measures were significantly poorer in the + VVM group: tonic EDA was lower ($t(417)=-4.31, p < 0.001$) and phasic EDA higher ($t(417) = 4.35, p < 0.001$). Postural accelerations varied across groups; LME models indicated a relationship between visual context, postural, and ANS responses in the + VVM group.

CONCLUSIONS

Lower tonic EDA with + VVM suggests canal-otolith dysfunction. The positive association between vertical acceleration, tonic EDA, and visual dependence suggests that increased vertical segmental adjustments are used to compensate. Visual context of the spatial environment emerged as an important variable to control when testing or treating VVM.

Introduction

Individuals presenting with non-specific dizziness are often sensitive to conflict between visual and vestibular signals. In fact, this sensitivity has been recognized in the International Classification of Vestibular Disorders by the Bárány Society as visual-vestibular mismatch (VVM).(1) VVM symptoms include false sensations of motion or tilting of the visual surround and visual distortion (blur) that are visually-induced and result from vestibular pathology or an unresolved conflict between visual and vestibular stimuli.(1)

Dizziness can be a challenge for clinicians to treat because of the absence of an objective biometric measure that can establish the criteria for diagnosis.(2, 3) A validated assessment of VVM does exist(4), but it has not been generally accepted as a reliable tool to identify presence of, or objectively characterize VVM. Objective criteria for rehabilitation and treatment for individuals with VVM have not been identified, and currently, treatment intensity is governed by anecdotal reports of dizziness. The lack of information about clinical progression likely affects the quality of rehabilitative care(5, 6) as individuals present with varying severity of dizziness, and the effectiveness of a treatment intervention may be dependent on its intensity.(7)

Our prior research revealed that a large proportion of individuals that have been diagnosed with vestibular migraine also test positive for VVM (57%) and visual dependency (42%).(8) This strong association between dizziness, visual dependence, and VVM implies that dysfunction in the autonomic nervous system (ANS) might also be contributing to these disorders of orientation.(9) Conversely, individuals with peripheral and central vestibular dysfunction have been shown to exhibit symptoms and signs of autonomic dysfunction.(10–13) Electrolytic or chemical lesions in the caudal region of the medial vestibular nucleus reduce vestibular-elicited activity in sympathetic nerve indicating that the vestibular system has a role in regulating ANS activities that maintain the stability of the human body's internal environment in response to changes in external conditions.(11, 14) Dizziness, nausea, and light headedness are autonomic signs that are elicited when the vestibular and visual stimuli are in conflict.(10)

Availability of physiologic and subjective findings of a strong relationship between ANS and vestibular symptoms suggest that responses of the ANS might serve as objective measures of VVM when in environments presenting mismatched or conflicting vestibular and visual signals. Sympathetic ANS responses can be assessed by using measures of electrodermal activity (EDA).(15–18)Thus, EDA(19) could provide an insight into the modulation of central sympathetic activities in individuals with VVM.

Another quantifiable output used to indicate disturbances in the vestibular system is postural sway. Individuals with unilateral and bilateral vestibular hypofunction tend to have greater sway area compared to healthy controls.(20) Connections between the vestibular nuclei and cerebellum, cerebellum and frontal eye fields, and vestibular nuclei to the parietal lobe likely contribute to the dizziness and disorientation evoked by VVM.(21–24) Integrating EDA and postural control measures might provide some insight into how the vestibular system and ANS are interrelated.

Our previous study (AlSharif et al., submitted) reported significant differences in EDA and postural behaviors in young adults with vestibular migraine compared with healthy young adults. In this study, we have chosen to further explore the changes in postural sway and EDA in individuals with vestibular migraine when exposed to visual and vestibular conflict.(25–28) We hypothesized that individuals with vestibular migraine who also exhibit symptoms of VVM will present with increased EDA and irregular postural sway compared to individuals with vestibular migraine without VVM when exposed to an immersive virtual reality (VR) environment that produces a visual-vestibular conflict.(29) In the attempt to identify a structure for future interventions, we have also explored whether the context of the environment (i.e., amorphous moving textures vs. meaningful moving images) influenced the magnitude of the EDA and postural responses.

Methods

Subjects

This study was approved by the Institutional Review Board of the Ministry of Health of the Kingdom of Saudi Arabia (protocol # H-05-FT-083). A convenience sample of 23 young adults with a previous diagnosis of vestibular migraine (34 ± 8 years old) who presented to the outpatient Otoneurology and Emergency Departments at Hafer Al-Batin Central hospital between the period of December 2020 and February 2021. Data from the healthy participants have been previously reported (Al Sharif et al., submitted).

Those willing to participate provided informed consent. Of those, 13 participants with vestibular migraine tested positive for VVM (+ VVM) and 10 tested negative for VVM (-VVM) on the Visual-Vestibular Mismatch Questionnaire (Table 1).(30) In a separate visit, vestibulonystagmography (bi-thermal caloric, positional nystagmus, smooth pursuit, random saccade, gaze stability, optokinetic nystagmus, and oculomotor testing was performed on all participants with migraine. Values of the abnormal caloric testing result were established by the clinical laboratory as a directional preponderance of 25% or greater.

Table 1
Demographic and clinical characteristics of participants with vestibular migraine (n = 23)

Variable		+VVM (13)	-VVM (10)
Gender			
	Female	10 (77%)	4 (40%)
	Male	3 (23%)	6 (60%)
Age (years)			
Mean ± SD		34 ± 9	34 ± 8
BMI (kg/m^2) ***			
Mean ± SD		30 ± 8	26 ± 5
Handedness			
	Right-handed	13 (100%)	9 (90%)
	Left-handed	–	1 (10%)
Rapid Assessment of Physical			
Activity	Active	4 (31%)	1 (10%)
	Under Active	8 (61%)	8 (80%)
	Sedentary	1 (8%)	1 (10%)
Activities of Balance Confidence ***			
Mean ± SD		71 ± 22	95 ± 12
RFT (Visual Dependency) Mean ± SD (Angle deviation) **		14 ± 4	10 ± 4
	Dependent	11 (85%)	8 (80%)
	Non-Dependent	2 (15%)	2 (20%)
Visual Vertigo Analog Scale ***			
Mean ± SD		52 ± 13	5 ± 10
Dizziness Handicap Inventory ***			
Mean ± SD		48 ± 24	9 ± 19
Vertigo Symptoms Scale-Short Form ***		14 ± 7	5 ± 6
Mean ± SD			

Variable		+VVM (13)	-VVM (10)
Origin	Vestibular	7 (54%)	1 (10%)
	Autonomic	6 (46%)	8 (80%)
	Both	–	1 (10%)

INSERT Table 1 **HERE**

Procedures

Participants stood on the center of a standard AIREX 20"x16.4"x2" balance pad (Advanced Medical Technology Inc., Watertown, MA) with their arms at their sides and their feet about shoulder-width apart. Participants were asked to maintain an upright standing position with their eyes open while wearing a head mounted display (HMD) and watching a virtual visual scene for 3 min. Each exposure to the dynamic visual environment was followed by a rest period of at least one min until any emerging symptoms of dizziness, nausea, or any discomfort were resolved.

Virtual Reality Environment. Participants were exposed to a three-dimensional complex visual environment generated by the software PosturoVR 0.8.3 (Virtualis, France) projected on the Oculus Rift HMD (Oculus Rift, CA). The field of view (FOV) of this device is more than 90 deg horizontal (110 deg on the diagonal). Vision of the real world is completely blocked providing a strong sense of immersion.

Two virtual environments (a space scene [SPACE] and a pedestrian crossing scene [STREET]) were randomly presented in one visit (Fig. 1). The SPACE scene was a projection of star-like objects at different sizes and distances from the participant that rotated in the yaw axis with no cues to vertical. This image has been previously demonstrated to induce strong sensations of self-motion during quiet stance.(31–33) The direction of motion was to the side of the dominant hand. The STREET scene was constructed of three-dimensional, recognizable objects (i.e., buildings, sidewalks, traffic signals, cars, pedestrians) that moved in multiple directions at varied distances from the participant.

INSERT FIGURE 1 **HERE**

Electrodermal Activity (EDA). EDA is a measure of skin conductance and consists of a (1) tonic component, also known as skin conductance level (SCL), which changes slowly over time (baseline) and indicates the active state of the sympathetic nervous system, and a (2) phasic component known as the skin conductance response (SCR) which changes rapidly in response to external new, unexpected, and/or arousal-driven stimuli (Al Sharif et al., submitted). Sudden shifts of phasic activity above the tonic activity indicate the SCR peaks.

Changes in EDA were recorded using the wireless Shimmer3 GSR + sensor unit (Shimmer-North America, Cambridge MA) that measures changes in skin conductivity produced by increases in the activity of sweat glands at a sampling rate of 128 Hz. The sensor was placed over the palmar surface of the medial

metacarpal-phalanges of the third and fourth fingers of the non-dominant hand. Participants were instructed to close their eyes and relax until the investigator observed that activity detected and displayed by the Shimmer sensor unit remained close to a baseline.

Postural Control. Trunk triaxial linear acceleration data were tracked with a Shimmer3 IMU wearable sensor with a sampling rate of 128 Hz placed over the L5 vertebral region.

Self-reported Outcomes Measures. The presence of VVM, dizziness, balance confidence, and the level of physical activity of each individual were evaluated at the beginning of the experiment using the following validated clinical tools: Visual-Vestibular Mismatch Questionnaire (VVMQ),(30) Visual Vertigo Analog Scale (VVAS),(34) Dizziness Handicap Inventory (DHI)(35), Vertigo Symptoms Scale-Short Form (VSS-SF) (36), Activities of Balance Confidence (ABC) scale(37), and Rapid Assessment of Physical Activity.(38)

The presence of visual dependency was tested with a Rod and Frame task (RFT) available on the PosturoVR 0.8.3 software (Virtualis, France) and projected on to the Oculus Rift. At the beginning of each trial, the virtual rod was set randomly at a 45-deg angle to the left or right. The rod was then slowly moved toward vertical by the investigator and the participant raised their hand to signal when they perceived that the rod had achieved a vertical position. The same procedure was repeated four times and the measure of angular deviation from vertical averaged for later analysis.

Data Analyses

EDA measures. Raw EDA data was processed with MATLAB R2020b (The MathWorks, Inc., Natick, Massachusetts, USA) using the Ledalab-toolbox V3.4.9 (www.ledalab.de) using continuous decomposition analysis (CDA) to decompose the skin conductance data into its phasic (SCR) and tonic (SCL) components.(39) The CDA method can be applied to full-length data which provides a complete decomposition model of the original data. All mathematical models of CDA are based on a physiological rationale to avoid underestimation biases due to overlapping responses. However, the integrated skin conductance response (ISCR), defined as the area (time integral) of the phasic component within the response window, reflects the phasic EDA response to a given event or stimulus. It equals SCR multiplied by the size of the response window [Microsiemens (μS) $*$ $\mathrm{seconds}(s)$]. The detection threshold for significant peaks was set to 0.01 μS as recommended by the Society for Psychophysiological Research. (17) To prevent the common skewed distribution of electrodermal response measures, the standardized ISCR was computed as(39):

$$ISCR = log(1 + |ISCR|) \times sign(ISCR)$$

Postural Acceleration Measures. Trunk linear acceleration data was processed using MATLAB R2020b (The MathWorks, Inc., Natick, Massachusetts, USA) which provides a formula for calculating the Root Mean Square (RMS) and the Normalized Path Length (NPL). RMS and NPL were calculated for the antero-posterior (AP), medio-lateral (ML), and vertical (Vert) planes where a higher value indicates greater postural instability.(40–43) RMS is the mean power of the entire trial time and NPL is the sum of the

absolute values of acceleration over time divided by the length of time that it takes to travel that distance, thus describing smoothness of the trunk motion. RMS and NPL were computed using the following formulae(44):

$$RMS = \sqrt{\left(\frac{\sum_{j=1}^{N-1} p_j}{N}\right)^2} \quad NPL = \frac{1}{t}\sum_{j=1}^{N-1} |p_{j+1} - p_j|$$

where t is time duration, N is the number of time samples, p_j is the acceleration data at time sample j. Data were low-pass filtered using a 4th order Butterworth filter with a cutoff frequency of 1.25 Hz. Each trial was plotted individually and inspected visually to ensure that the data were free from significant artifacts.

Statistical Analyses

EDA and six postural acceleration measures (RMS and NPL each in ML, AP, and Vert axes) were analyzed using R version 4.0.4 (R Foundation for Statistical Computing, Vienna, Austria). Correlations for continuous variables were computed with Pearson correlation coefficients and a two-tailed test. A Shapiro-Wilk test revealed the data were normally distributed.

Linear mixed-effects (LME) models were constructed to statistically assess the effects of the virtual visual environments (SPACE and STREET) across groups (+ VVM and -VVM) and time. Response variables included ISCR, NPL, and RMS with the subject as a random effect with a slope fit for each trial. LME models were fit using restricted maximum likelihood.(45) After examining the full-effects model for EDA phasic, EDA tonic, RMS, and NPL responses in the AP, ML, and Vert planes, non-significant terms and interactions were removed. The final model for estimating the change in EDA phasic response included the interaction of group with time.

Specific differences between the virtual environments and groups were examined with a Wilcoxon signed rank test. Cohen's d (range 0-1.4) was used to calculate effect sizes of differences between group means. Relative effect sizes were categorized as small (d = 0.2), medium (0.5), and large (0.8).(46)

Data from self-reported outcome measures were analyzed using IBM SPSS Statistics v.23 (IBM Corporation, Armonk, N.Y., USA) and reported as mean ± standard deviation or as a percentage of participants. The significance level was set at $\alpha = 0.05$ for all analyses. Bonferroni post-hoc adjustments were used to adjust for multiple comparisons. Differences in demographics and clinical outcome scores between the + VVM and -VVM groups were assessed using Welch's t-test. Individuals were assigned positive or negative results on the RFT based on the criterion of an angle of deviation greater than 5 deg to indicate visual dependency.(8)

Results

Self-Reported Outcome Measures

Significant differences were observed on the ABC, VVAS, DHI, and VSS-SF measures (Table 1). The + VVM group had significantly lower scores on the ABC than the -VVM group ($t(131.85) = 12.07$, $p < 0.001$). Additionally, the -VVM adults exhibited significantly lower (better) scores than the + VVM group on the DHI, the VVAS, and the VSS-SF ($t_{DHI}(174.54) = -17.12$, $t_{VVAS}(166.68) = -36.52$, $t_{VSS\text{-}SF}(197.44) = -13.26$, all $p < 0.001$).

RFT testing indicated that 85% of individuals in the + VVM and 80% of individuals in the -VVM group tested positive for visual dependence; because this result was not significantly different, the impact of visual dependence was not explored further. It should be noted, however, that the angle of deviation from vertical reported on the RFT was significantly higher for the + VVM group than the -VVM group ($t(23.30) = -3.11$, $p = 0.004$).

Postural Acceleration Measures

The six postural acceleration measures (i.e., RMS and NPL each in ML, AP, and Vert axes) exhibited large variability between the two groups across the three minutes of exposure to the VR environment (Fig. 2). A Wilcoxon signed-rank test revealed significant differences across time between the + VVM and -VVM groups mostly in the vertical plane of motion. There was also a significant difference with a high effect size at the initiation of STREET motion in the RMS-ML ($W = 94$, $p = 0.01$, $d = 0.87$) and NPL-ML ($W = 119$, $p = 0.01$, $d = 0.83$) measures.

INSERT FIGURE 2 **HERE**

RMS and NPL measures in the AP and ML directions did not exhibit significant differences with either environment (Table 2). There were differing effects of the SPACE and STREET environments on the RMS-Vert measures of the two groups (Fig. 2). Although not statistically different, a medium effect size was observed in the RMS-Vert group means in the SPACE ($t(40) = -2.30$, $p = 0.02$, $d = 0.78$) and a large effect size in the STREET ($t(40) = -2.63$, $p = 0.01$, $d = 0.89$) environments. Significant differences between groups were also seen in NPL-Vert with medium to large effect sizes across the whole trial period during both SPACE ($t(40) = -2.54$, $p = 0.01$, $d = 0.87$) and STREET ($t(40) = -3.02$, $p = 0.004$, $d = 1.03$) environments (Fig. 2 and Table 3).

Table 2
Means ± standard deviation (SD) and statistical comparisons of postural measures across the two groups for the whole trial in each of the two virtual scenes.

		+VVM	*-VVM*		
Measure	Scene	Mean ± SD	Mean ± SD	t -statistic	p-value
RMS AP	Space	12.65 ± 5.96	12.23 ± 6.71	-0.18	0.85
	Street	12.00 ± 7.85	12.27 ± 7.65	0.14	0.88
RMS ML	Space	10.67 ± 3.56	10.21 ± 5.86	-0.13	0.89
	Street	11.10 ± 2.67	9.37 ± 7.46	-0.81	0.42
RMS Vert	Space	**8.93 ± 8.92**	**4.16 ± 2.00**	**-2.30**	**0.02**
	Street	**7.96 ± 9.64**	**4.01 ± 6.78**	**-2.63**	**0.01**
NPL AP	Space	11.50 ± 4.59	10.14 ± 7.98	-0.67	0.50
	Street	10.62 ± 5.06	9.72 ± 10.28	-0.60	0.54
NPL ML	Space	10.34 ± 3.42	9.19 ± 4.85	-0.39	0.69
	Street	10.49 ± 5.64	7.49 ± 5.40	-1.71	0.09
NPL Vert	Space	**9.36 ± 8.20**	**4.13 ± 2.73**	**-2.54**	**0.01**
	Street	**7.85 ± 8.91**	**3.60 ± 4.47**	**-3.02**	**0.004**

Positive VVM (+ VVM); Negative VVM (-VVM); significant values in bold.

Table 3
Confidence Interval and Effect Size of NPL-Vert with respect to time in the two visual environments.

Scene	Statistic	0 min	1 min	2 min	3 min	End
SPACE	*p*-value	**0.02***	**0.01****	**0.01****	**0.03***	**0.01****
	CI 95%	-2.98, -0.21	-6.44, -0.67	-5.45, -0.42	-4.90, -0.17	-4.12, -0.68
	Effect size	0.69 (Medium)	0.90 (Large)	0.94 (Large)	0.72 (Medium)	0.79 (Medium)
STREET	*p*-value	0.12	**0.005*****	**0.02****	**0.006*****	**0.009*****
	CI 95%	-3.47, 0.36	-5.52, -0.68	-4.85, -0.31	-5.54, -0.89	-4.41, -0.72
	Effect size	0.56 (Medium)	1.10 (Large)	0.91 (Large)	1.03 (Large)	0.91 (Large)
* p < 0.05 ** p < 0.01 *** p < 0.001						

INSERT Table 2 **HERE**

INSERT Table 3 **HERE**

EDA Measures

The -VVM group presented with higher tonic levels of EDA than the + VVM group (Fig. 3). A significant fixed effect of time was observed ($F(4,417) = 4.57$, $p = 0.001$) where the + VVM group exhibited an estimated − 0.48 μS less EDA tonic activity than the -VVM group ($t(417) = -4.31$, $p < 0.001$). With both virtual environments, tonic EDA responses of the -VVM group were highest at the initiation of a trial and then dropped below zero by the end of a trial.

INSERT FIGURE 3 **HERE**

A significant fixed effect of time was also observed on the phasic EDA response ($F(4,417) = 6.47$, $p < 0.001$). The phasic EDA response in the + VVM group was approximately 0.82 μS greater than the -VVM group ($t(417) = 4.35$, $p < 0.001$). In both virtual environments, the + VVM group started with a lower baseline phasic EDA level than the -VVM group (Fig. 3) that was only significant for the SPACE scene ($W = 91$, $p = 0.03$, $d = 1.05$). In the first minute of exposure to virtual scene motion, the phasic EDA response of the + VVM group rose to that of the -VVM group. At the end of the trial, the -VVM group phasic EDA activity dropped to close to the level of the + VVM group (see Fig. 3).

Effect of Visual Context

The relationship between the visual environment and the dependent variables (RMS and NPL in the ML, AP, and Vert axes and phasic ISCR and tonic EDA) was explored with LME models constructed to

statistically assess the effects of the virtual environments (SPACE and STREET) across groups (+ VVM and -VVM) and time. Results indicated an effect of the STREET environment on trunk motion in the vertical plane (Table 4).

Table 4
Linear Mixed Model results of time, +VVM, and virtual environment

Terms	*Factors*	*Sum Sq.*	*Mean Sq.*	*Num df*	*Den df*	*F value*
ISCR Phasic Response	+VVM	0.02	0.02	1	417	0.03
	Time	45.79	11.44	4	417	**18.03*** **
	+VVM*Time	16.43	4.10	4	417	**6.47*** **
Tonic Response	+VVM	0.01	0.01	1	417	0.008
	Time	13.77	3.44	4	417	**4.57** **
	+VVM*Time	5.66	1.41	4	417	1.88
NPL AP	+VVM	0.01	0.01	1	37.21	0.001
	Time	71.27	17.81	4	365.46	**2.69***
	STREET Scene	34.67	34.67	1	364.92	**5.25***
	+VVM*Time	56.32	14.08	4	365.46	2.13
NPL ML	+VVM	7.63	7.63	1	40.16	0.46
	Time	235.72	58.93	4	370.05	**3.60** **
	STREET Scene	127.20	127.20	1	368.69	**7.79** **
	+VVM*Time	78.94	19.73	4	370.05	1.20
NPL VERT	+VVM	15.73	15.73	1	41.20	**4.76***
	Time	43.56	10.89	4	369.70	**3.29***
	STREET Scene	45.28	45.28	1	369.35	**13.70*** **
	+VVM*Time	32.26	8.06	4	369.70	**2.44***
RMS AP	+VVM	3.24	3.23	1	23.21	0.16
	Time	103.04	25.76	4	359.00	1.34
	STREET Scene	9.92	9.92	1	358.09	0.51
	+VVM*Time	112.07	28.01	4	359.00	1.46
RMS ML	+VVM	4.43	4.42	1	41.84	0.15
	Time	411.06	102.76	4	372.99	**3.49** **

Positive (+) VVM (visual-vestibular mismatch); Time of exposure to scene motion (Time); Integrated skin conductance response (ISCR); Root mean square (RMS); Normalized path length (NPL); Anteroposterior (AP); Mediolateral (ML); Vertical (Vert). * $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

Terms	*Factors*	*Sum Sq.*	*Mean Sq.*	*Num df*	*Den df*	*F value*
	+VVM*Time	103.97	25.99	4	372.99	0.88
RMS VERT	+VVM	11.99	11.99	1	40.73	2.93
	STREET Scene	18.30	18.30	1	375.78	**4.47***
	+VVM*STREET Scene	6.13	6.13	1	375.78	1.50

Positive (+) VVM (visual-vestibular mismatch); Time of exposure to scene motion (Time); Integrated skin conductance response (ISCR); Root mean square (RMS); Normalized path length (NPL); Anteroposterior (AP); Mediolateral (ML); Vertical (Vert). * $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

INSERT Table 4 **HERE**

Plotting postural responses against EDA (Fig. 4), reveals a possible relationship between visual context, postural, and ANS responses in the + VVM group that is not as evident in the -VVM group. With + VVM, there is an associated increase in tonic EDA responses and NPL-Vert responses in the STREET scene; ISCR phasic responses of the + VVM group also suggest this association in the SPACE scene. In contrast, there is a distinct decrease in NPL-Vert responses as tonic EDA responses increase in the SPACE scene.

A significant fixed effect for STREET on NPL-Vert ($F(1,360.30) = 19.72$, $p < 0.001$) revealed an estimated 4.29 μS increase in the + VVM group compared to the -VVM group ($t(42) = 2.45$, $p = 0.01$). In the other planes, NPL values are lower in the + VVM than in -VVM group. The estimated fixed effect revealed that NPL-AP with the STREET scene was approximately − 0.57 μS less in the + VVM than the -VVM group ($t(364) = -2.29$, $p = 0.02$); NPL-ML was − 1.09 μS less in the + VVM than -VVM group ($t(368) = -2.69$, $p = 0.005$).

INSERT FIGURE 4 **HERE**

Discussion

We have previously shown that the EDA activity and postural sway acceleration responses within a VR environment produced distinct behaviors that could be used to distinguish between adults with vestibular migraine and healthy adults (Alsharif et al., submitted). The current study explored whether different visual contexts might further discriminate between those adults having vestibular migraine with or without VVM. We hypothesized that a STREET environment would trigger stronger symptoms, and thus, larger EDA and postural responses, than the SPACE environment because it presents a recognizable visual scene with identifiable cues to spatial orientation.(20)

Individuals testing positive for VVM responded with more frequent postural accelerations in the vertical plane than the -VVM group. In the STREET environment, these frequent postural adjustments were positively associated with larger tonic EDA. In the SPACE environment, however, postural adjustments

decreased as tonic EDA increased. An association between increased tonic EDA and improved postural performance has been previously reported. Individuals with high levels of EDA tonic activity exhibited better balance confidence and reduced center of pressure displacement during postural compensatory responses to sudden external perturbations.(23, 24, 47, 48)High EDA tonic activity was also found to be positively correlated with higher ABC scores indicative of better postural stability and less severe dizziness (AlSharif et al., submitted). Our findings imply that the STREET environment supported the attainment of postual control and spatial orientation in individuals with VVM, likely due to the presence of recognizable objects and cues to vertical. Conversely, the SPACE environment presented more challenges for resolving visual-vestibular conflict because of the nebulous visual context and the absence of cues to vertical. Future studies may choose to focus on exploring the correlation between characteristics of virtual environments and these self-reported outcome measures to establish a threshold-tolerance concept basis for designing a vestibular rehabilitation program that will more precisely target symptom severity.

Results of this study extend the role of the ANS in postural control to attenuating symptoms of visual motion sensitivity during exposure to complex visual environments in functional activities. Tonic EDA is reflective of a level of central excitation (i.e., central set) that provides a readiness for disturbances that are expected to occur. Thus, lower tonic EDA levels exhibited by the + VVM group at the intiation of each trial may be indicative of a canal-otolith dysfunction. Phasic EDA is the response to a given event. The highest level of phasic ISCR occurred with the initial projection of the VR environment in both groups and then quickly dropped off. This would suggest that either group was capable of mediating an online process for matching the anticipated event with what actually did occur in the environment. These findings align with prior evidence that canal-otolith function is strongly linked to anticipatory and compensatory postural control.(49, 50)

Our results also align with previous reports of visual dependency in individuals with vestibular migraine. (8) Although all participants exhibited visual dependency, it is of interest that those in the + VVM group also produced the largest deviations from vertical orientation in the RFT. The RFT is a validated tool for otolith-utricular assessment as it measures the degree to which a subject uses available visual cues to locate gravitational vertical.(51, 52)These findings suggest the possibility of canal-otolith dysfunction in + VVM adults. The positive association emerging between vertical acceleration and visual dependence could imply a compensation for this canal-otolith dysfunction by increasing vertical segmental adjustments in order to achieve a perception of verticality.

Controlling both visual context and complexity of the spatial environment emerges from these findings as important task variables to consider with individuals suspected of having VVM. Previous evidence has shown that the amount of uncertainty in visual stimuli strongly influences the amount of induced postural instability.(20) Motion of the visual environment was less complex in the SPACE environment as it was presented only in the yaw plane, however, the absence of visual cues to vertical presented a challenge to individuals with VVM. The STREET environment contained multiplanar motion, however it provided recognizable contexts of a street with 3D objects at randomly generated heights, moving cars,

and walking pedestrians. Projection of immersive contextual environments with moving avatars has been shown to elicit distinct postural sway behaviors in people with vestibular disorders.(53) The STREET environment projected a flow of pedestrians appearing to move toward, away, and next to the participants, which then induced frequent postural adjustments even though there were recognizable cues to vertical.

There were some limitations of the study. First, the cervical vestibular evoked myogenic potential (cVEMP) and the ocular vestibular evoked myogenic potential (oVEMP) assessments were not available which limited our ability to confirm integrity of otolith function. Because of COVID-19 restrictions, this study was limited in sample size and recruitment sites which could limit the generalizability of our findings. Finally, we assessed only static balance control. Future studies that integrate assessment of dynamic balance tasks and measures may provide further insights into the impact of VVM in adults with vestibular disorders.

INSERT FIGURE 5 **HERE**

Nevertheless, the results of this study have the potential to advance our understanding of the behavioral impact of dizziness with VVM and to shape guidelines to customize visual environmental demands in vestibular rehabilitation. A conceptual model has been developed that encapsulates the main results of this study and suggests future directions for intervention (Fig. 5). This schematic illustrates the importance of both the vestibular (canal-otolith) system and the autonomic nervous system to compensatory postural control.

Our results indicate that the scores from subjective outcome measures combined with measures of tonic EDA activity can provide a meaningful indication of otolith function. The integrity of the otolith organs influences CNS integration processes and, therefore, the ability to produce successful compensatory postural responses. Dysfunction in the otolith organs results in an inaccurate perception of vertical orientation. Segmental adjustments (as were measured through trunk accelerations) were influenced by perception of the visual environment and can be used to enhance somatosensory feedback. This would overwhelm canal-otolith disinformation and ultimately produce successful postural behaviors.

Declarations

Ethics approval and consent to participate

All procedures performed in this study with human participants were in accordance with the ethical standards of the institutional research board committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication

This included obtaining informed parental consent for all participants.

Availability of data and materials

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

All authors declare that they have no competing interests.

Authors' contributions

DA and EK were responsible for the conception and design of the study. The data were analyzed by DA. DA drafted the manuscript and EK (corresponding author) provided substantial input to the first draft. DC provided intellectual input to interpretation of the results and drafting of the manuscript. CT and DC provided intellectual input into the final draft of the manuscript. All authors reviewed the manuscript and gave final approval of the version to be submitted. The study was supervised by EK. All authors read and approved the final manuscript.

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References

1. Bisdorff AR, Staab JP, Newman-Toker DE. Overview of the International Classification of Vestibular Disorders. Neurologic Clinics [Internet]. 2015 Aug;33(3):541–50. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26231270
2. Welgampola MS, Bradshaw AP, Lechner C, Halmagyi GM. Bedside Assessment of Acute Dizziness and Vertigo. Neurologic Clinics [Internet]. 2015 Aug;33(3):551–64. Available from: http://dx.doi.org/10.1016/j.ncl.2015.04.001
3. Sealy A. Vestibular assessment: a practical approach. Occup Med (Lond) [Internet]. 2014 Mar;64(2):78–86. Available from: http://dx.doi.org/10.1093/occmed/kqt153
4. Longridge NS, Mallinson AI. Visual vestibular mismatch in whiplash and Ménière's disease. In excerpta MEDICA INTERNATIONAL CONGRESS SERIES 2000 Jan 1 (Vol. 1201, No. 1, pp. 397–402). Elsevier.
5. Hoffer ME, Schubert MC, Balaban CD. Early Diagnosis and Treatment of Traumatic Vestibulopathy and Postconcussive Dizziness. Neurologic Clinics [Internet]. 2015 Aug;33(3):661–8. Available from: http://dx.doi.org/10.1016/j.ncl.2015.04.004

6. van Ombergen A, Lubeck AJ, van Rompaey V, Maes LK, Stins JF, van de Heyning PH, et al. The Effect of Optokinetic Stimulation on Perceptual and Postural Symptoms in Visual Vestibular Mismatch Patients. Glasauer S, editor. PLOS ONE [Internet]. 2016 Apr 29;11(4):e0154528. Available from: https://dx.plos.org/10.1371/journal.pone.0154528
7. Cabrera Kang C, Tusa R. Vestibular Rehabilitation: Rationale and Indications. Seminars in Neurology [Internet]. 2013 Sep 21;33(03):276–85. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24057831
8. Al-Sharif DS, Roehm P, Lindemann TL, Dumenci L, Keshner EA. Visual-vestibular mismatch correlates with headache. Journal of Vestibular Research. 2021 Jan;31:173–80.
9. Staab JP, Ruckenstein MJ. Autonomic nervous system function in chronic dizziness. Otol Neurotol [Internet]. 2007 Sep;28(6):854–9. Available from: https://journals.lww.com/00129492-200709000-00023
10. Balaban CD. Vestibular autonomic regulation (including motion sickness and the mechanism of vomiting). Current Opinion in Neurology [Internet]. 1999 Feb;12(1):29–33. Available from: http://journals.lww.com/00019052-199902000-00005
11. Furman JM, Jacob RG, Redfern MS. Clinical Evidence That the Vestibular System Participates in Autonomic Control. Journal of Vestibular Research [Internet]. 1998 Feb 1;8(1):27–34. Available from: https://www.medra.org/servlet/aliasResolver?alias=iospress&doi=10.3233/VES-1998-8104
12. Özer G. Presence of Symptoms of Dysautonomia in Patients with Migraine with Aura and Migraine without Aura: A Retrospective Study. Eurasian Journal of Medical Investigation [Internet]. 2018 [cited 2021 May 30];2(4):209–12. Available from: www.ejmi.org
13. Pappas DG. Autonomic related vertigo. Laryngoscope [Internet]. 2003 Oct 3;113(10):1658–71. Available from: http://doi.wiley.com/10.1097/00005537-200310000-00005
14. Topoglu Y, Watson J, Suri R, Ayaz H. Electrodermal activity in ambulatory settings: a narrative review of literature. Advances in Intelligent Systems and Computing. 2019 June;953:91–102.
15. Tamura A, Iwamoto T, Ozaki H, Kimura M, Tsujimoto Y, Wada Y. Wrist-Worn Electrodermal Activity as a Novel Neurophysiological Biomarker of Autonomic Symptoms in Spatial Disorientation. Frontiers in Neurology [Internet]. 2018 Dec 4;9:1–11. Available from: https://www.frontiersin.org/article/10.3389/fneur.2018.01056/full
16. Braithwaite JJ, Watson DG, Jones R, Rowe M. A Guide for Analysing Electrodermal Activity (EDA) & Skin Conductance Responses (SCRs) for Psychological Experiments {via the Biopac MP36R & AcqKnowledge software}. Psychophysiology. 2013 Jan;49(8):1017–34.
17. Boucsein W, Fowles DC, Grimnes S, Ben-Shakhar G, Roth WT, Dawson ME, et al. Publication recommendations for electrodermal measurements. Psychophysiology [Internet]. 2012 Aug;49(8):1017–34. Available from: https://onlinelibrary.wiley.com/doi/10.1111/j.1469-8986.2012.01384.x
18. Caruelle D, Gustafsson A, Shams P, Lervik-Olsen L. The use of electrodermal activity (EDA) measurement to understand consumer emotions – A literature review and a call for action. Journal

of Business Research. 2019 Nov 1;104:146–60.

19. Vijaya PA, Shivakumar G. Galvanic skin response: a physiological sensor system for affective computing. International journal of machine learning and computing. 2013 Feb 1;3(1):31.
20. Kalla R, Muggleton N, Spiegel R, Bueti D, Claassen J, Walsh V, et al. Adaptive motion processing in bilateral vestibular failure. J Neurol Neurosurg Psychiatry [Internet]. 2011 Nov 1;82(11):1212–6. Available from: https://jnnp.bmj.com/lookup/doi/10.1136/jnnp.2010.235960
21. Barthelemy J, Xerri C, Borel L, Lacour M. Experimental Brain Research Neuronal coding of linear motion in the vestibular nuclei of the alert cat II. Response characteristics to vertical optokinetic stimulation. Vol. 70, Exp Brain Res. 1988 April;70(2):287–98.
22. Ventre-Dominey J. Vestibular function in the temporal and parietal cortex: distinct velocity and inertial processing pathways. Frontiers in Integrative Neuroscience. 2014;8(July):1–13.
23. Wiest G. The origins of vestibular science. Ann N Y Acad Sci. 2015 April;1343(1):1–9.
24. Chang C-J, Yang T-F, Yang S-W, Chern J-S. Cortical Modulation of Motor Control Biofeedback among the Elderly with High Fall Risk during a Posture Perturbation Task with Augmented Reality. Frontiers in Aging Neuroscience [Internet]. 2016 Apr 28;8:1–13. Available from: http://journal.frontiersin.org/Article/10.3389/fnagi.2016.00080/abstract
25. Bronstein AM. Visual vertigo syndrome: clinical and posturography findings. J Neurol Neurosurg Psychiatry [Internet]. 1995 Nov 1 [cited 2021 May 25];59(5):472–6. Available from: https://jnnp.bmj.com/lookup/doi/10.1136/jnnp.59.5.472
26. Hafström A, Fransson PA, Karlberg M, Magnusson M. Idiosyncratic compensation of the subjective visual horizontal and vertical in 60 patients after unilateral vestibular deafferentation. Acta Oto-Laryngologica. 2004 Mar;124(2):165–71.
27. Zorzin L, Carvalho GF, Kreitewolf J, Teggi R, Pinheiro CF, Moreira JR, et al. Subdiagnosis, but not presence of vestibular symptoms, predicts balance impairment in migraine patients – a cross sectional study. The Journal of Headache and Pain [Internet]. 2020 Dec 24;21(1):56. Available from: https://thejournalofheadacheandpain.biomedcentral.com/articles/10.1186/s10194-020-01128-z
28. Sharma R, Goel D, Srivastav M, Dhasmana R.Differences in Heart Rate and Galvanic Skin Response among Nurses Working in Critical and Non-critical Care Units.J Clin of Diagn Res.2018 Nov; 12(11):CC09-CC12. https://www.doi.org/10.7860/JCDR/2018/35602/12244
29. Keshner EA, Kenyon RV. The influence of an immersive virtual environment on the segmental organization of postural stabilizing responses. Journal of Vestibular Research [Internet]. 2000 Nov 1;10(4–5):207–19. Available from: https://www.medra.org/servlet/aliasResolver?alias=iospress&doi=10.3233/VES-2000-104-505
30. Longridge NS, Mallinson AI. Visual Vestibular Mismatch in Work-Related Vestibular Injury. Otology & Neurotology [Internet]. 2005 Jul;26(4):691–4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16015170
31. Nesti A, Beykirch KA, Pretto P, Bülthoff HH. Self-motion sensitivity to visual yaw rotations in humans. Experimental Brain Research [Internet]. 2015 Mar 16;233(3):861–9. Available from:

http://link.springer.com/10.1007/s00221-014-4161-0

32. Grabherr L, Nicoucar K, Mast FW, Merfeld DM. Vestibular thresholds for yaw rotation about an earth-vertical axis as a function of frequency. Exp Brain Res [Internet]. 2008 Apr 19;186(4):677–81. Available from: http://link.springer.com/10.1007/s00221-008-1350-8
33. Riecke BE, Jordan JD. Comparing the effectiveness of different displays in enhancing illusions of self-movement (vection). Frontiers in Psychology [Internet]. 2015 Jun 1 [cited 2021 May 22];6(JUN):713. Available from: www.frontiersin.org
34. Dannenbaum E, Chilingaryan G, Fung J. Visual vertigo analogue scale: an assessment questionnaire for visual vertigo. J Vestib Res. 2011 Jun;21:153–9.
35. Jacobson GP, Newman CW. The development of the dizziness handicap inventory. Arch Otolaryngol Head Neck Surg [Internet]. 1990;116(4):424–7. Available from: http://dx.doi.org/10.1001/archotol.1990.01870040046011
36. Yardley L, Masson E, Verschuur C, Haacke N, Luxon L. Symptoms, anxiety and handicap in dizzy patients: development of the vertigo symptom scale. J Psychosom Res [Internet]. 1992 Dec;36(8):731–41. Available from: https://linkinghub.elsevier.com/retrieve/pii/002239999290131K
37. Moore DS, Ellis R, Kosma M, Fabre JM, McCarter KS, Wood RH. Comparison of the validity of four fall-related psychological measures in a community-based falls risk screening. Res Q Exerc Sport [Internet]. 2011 Sep;82(3):545–54. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21957713
38. Topolski TD, LoGerfo J, Patrick DL, Williams B, Walwick J, Patrick MB. The Rapid Assessment of Physical Activity (RAPA) among older adults. Prev Chronic Dis [Internet]. 2006 Oct;3(4):A118. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16978493
39. Benedek M, Kaernbach C. A continuous measure of phasic electrodermal activity. Journal of Neuroscience Methods. 2010 Jun;190(1):80–91.
40. Alqahtani BA, Sparto PJ, Whitney SL, Greenspan SL, Perera S, Brach JS. Psychometric properties of instrumented postural sway measures recorded in community settings in independent living older adults. BMC Geriatrics. 2020 Feb 28;20(1).
41. Salisbury JP, Keshav NU, Sossong AD, Sahin NT. Standing balance assessment using a head-mounted wearable device [Internet]. bioRxiv. 2017. Available from: http://dx.doi.org/10.1101/149831
42. Marchetti GF, Bellanca J, Whitney SL, Lin JC-C, Musolino MC, Furman GR, et al. The development of an accelerometer-based measure of human upright static anterior- posterior postural sway under various sensory conditions: test-retest reliability, scoring and preliminary validity of the Balance Accelerometry Measure (BAM). J Vestib Res [Internet]. 2013 Nov 1;23(4–5):227–35. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24284603
43. Alkathiry AA, Sparto PJ, Freund B, Whitney SL, Mucha A, Furman JM, et al. Using accelerometers to record postural sway in adolescents with concussion: A cross-sectional study. Journal of Athletic Training. 2018 December;53(12):1166–72.
44. Alqahtani BA, Sparto PJ, Whitney SL, Greenspan SL, Perera S, Brach JS. Psychometric properties of instrumented postural sway measures recorded in community settings in independent living older

adults. BMC Geriatr [Internet]. 2020 Feb;20(1):82. Available from: http://dx.doi.org/10.1186/s12877-020-1489-0

45. Baayen RH, Davidson DJ, Bates DM. Mixed-effects modeling with crossed random effects for subjects and items. Journal of Memory and Language [Internet]. 2008 Nov;59(4):390–412. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0749596X07001398
46. Cohen J. Statistical Power Analysis for the Behavioral Sciences [Internet]. 2nd Editio. Statistical Power Analysis for the Behavioral Sciences. New York, NY: Routledge; 1988. 567 p. Available from: https://books.google.com/books?id=rEe0BQAAQBAJ
47. Phillips J, Longridge N, Mallinson A, Robinson G. Migraine and vertigo: A marriage of convenience? Headache. 2010 Sep;50(8):1362–5.
48. Anagnostou E, Gerakoulis S, Voskou P, Kararizou E. Postural instability during attacks of migraine without aura. European Journal of Neurology. 2019 Feb;26(2):319-e21.
49. Sibley KM, Mochizuki G, Frank JS, McIlroy WE. The relationship between physiological arousal and cortical and autonomic responses to postural instability. Exp Brain Res [Internet]. 2010 Jun 28;203(3):533–40. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20424830
50. Horak FB, Nashner LM. Central programming of postural movements: adaptation to altered support-surface configurations. J Neurophysiol [Internet]. 1986 Jun 1 [cited 2021 May 25];55(6):1369–81. Available from: http://www.ncbi.nlm.nih.gov/pubmed/3734861
51. Vuralli D, Yildirim F, Akcali DT, Ilhan MN, Goksu N, Bolay H. Visual and Postural Motion-Evoked Dizziness Symptoms Are Predominant in Vestibular Migraine Patients. Pain Medicine [Internet]. 2017 Feb; 178–83. Available from: https://academic.oup.com/painmedicine/article-lookup/doi/10.1093/pm/pnx182
52. Bagust J, Docherty S, Haynes W, Telford R, Isableu B. Changes in Rod and Frame Test Scores Recorded in Schoolchildren during Development-A Longitudinal Study. PLoS ONE [Internet]. 2013May;8(5):65321. Available from: www.plosone.org
53. Lubetzky A v., Kelly JL, Hujsak BD, Liu J, Harel D, Cosetti M. Postural and Head Control Given Different Environmental Contexts. Frontiers in Neurology. 2021;12(June):1–13.

Figures

Figure 1

Images of the SPACE (***left***) and STREET (***right***) virtual scenes.

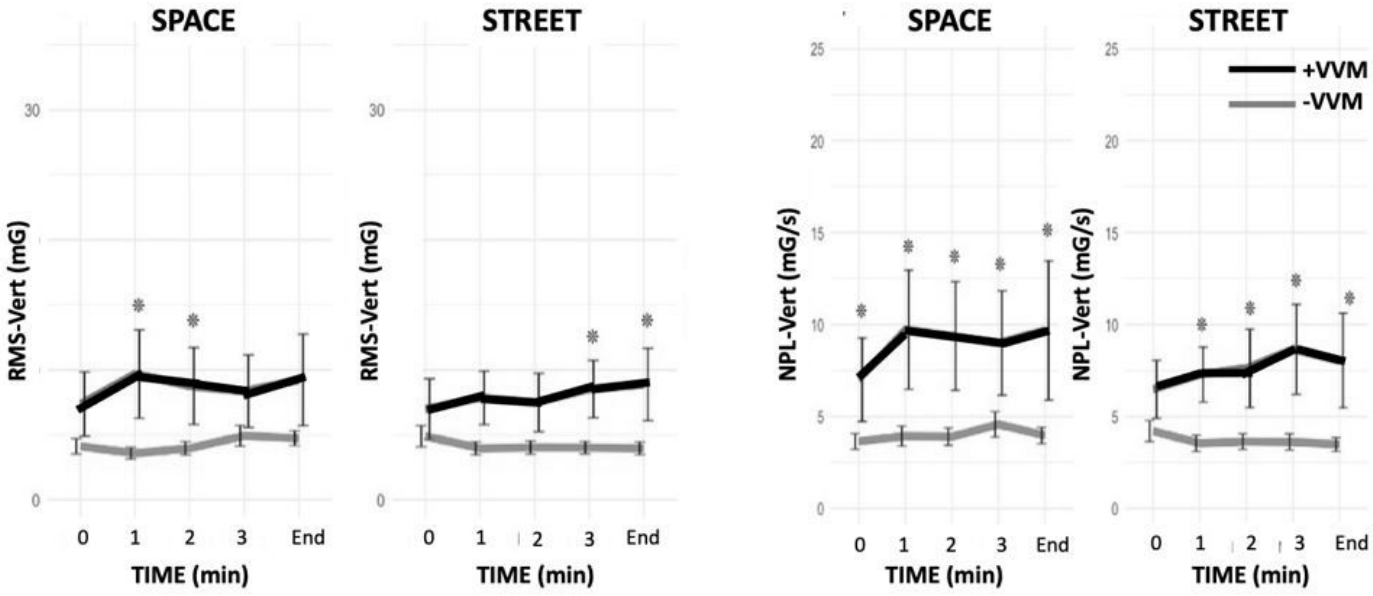

Figure 2

Mean and standard deviations of the RMS (***left***) and NPL (***right***) responses in the vertical plane for the +VVM (*black line*) and -VVM (*grey line*) participants across the period of the trial during the two visual

motion scenes (SPACE and STREET). An asterisk (*) indicates a statistically significant difference between groups (see Table 3 for values).

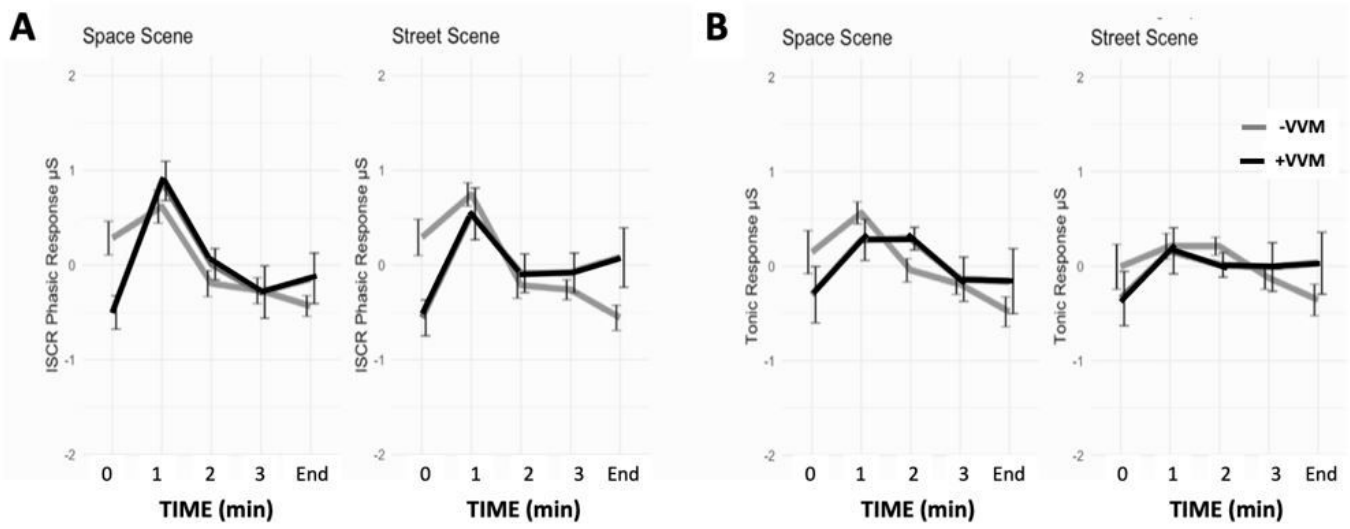

Figure 3

A. Phasic (EDA ISCR responses of the +VVM positive (*black line*) and -VVM (*grey line*) groups across the trial period of the virtual SPACE and STREET environments. ***B.*** Tonic EDA responses of the +VVM positive (*black line*) and -VVM (*grey line*) groups across trial period of the virtual SPACE and STREET environments.

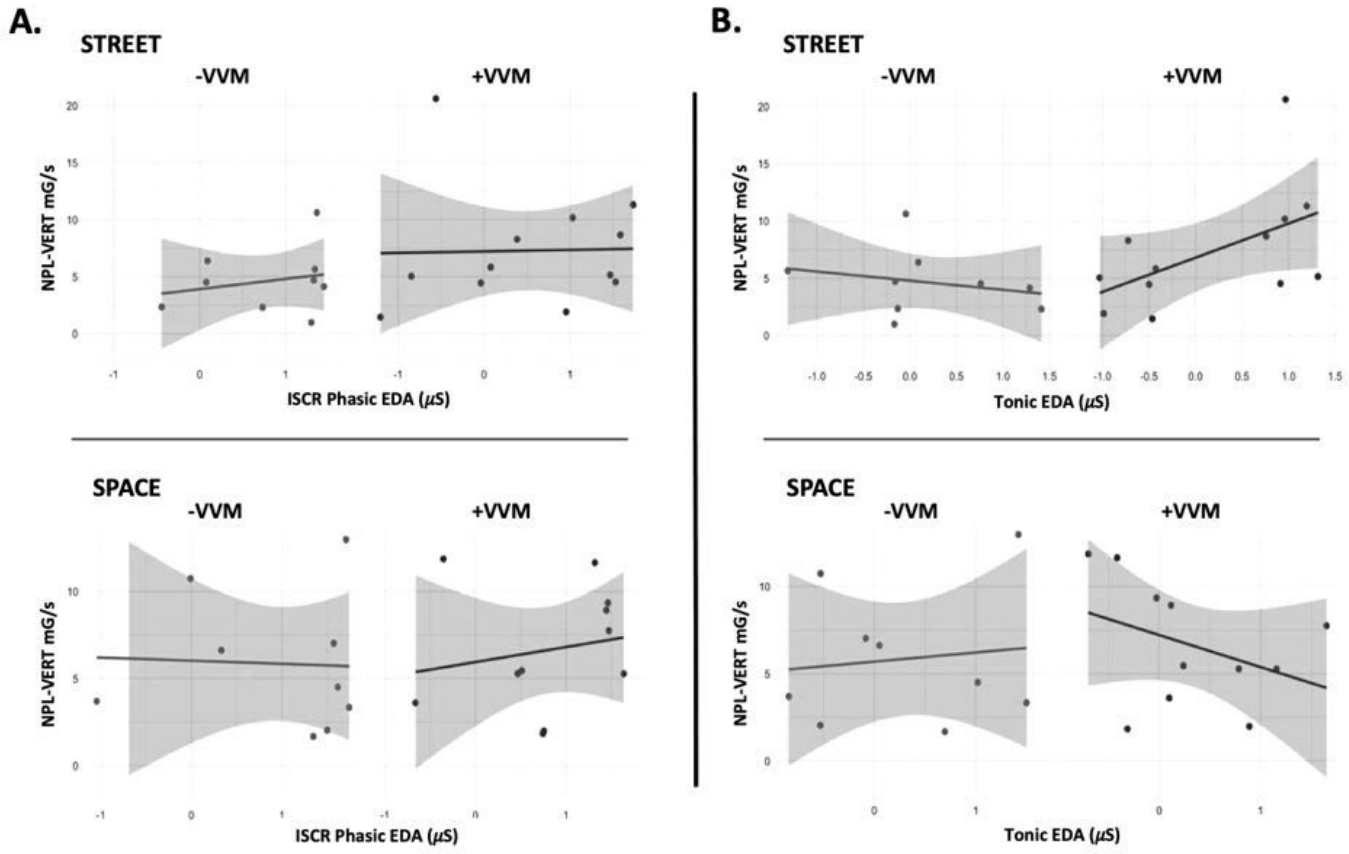

Figure 4

(***A***) ISCR phasic and (***B***) tonic electrodermal activity (EDA) (*x-axis*) plotted against normalized path length (NPL) of trunk acceleration in the vertical direction (*y-axis*) while viewing the STREET (top 2 graphs) or SPACE (bottom 2 graphs) virtual environment. Scatterplot on the left in each graph portrays responses of the -VVM group; scatterplot on the right portrays responses of the +VVM group.

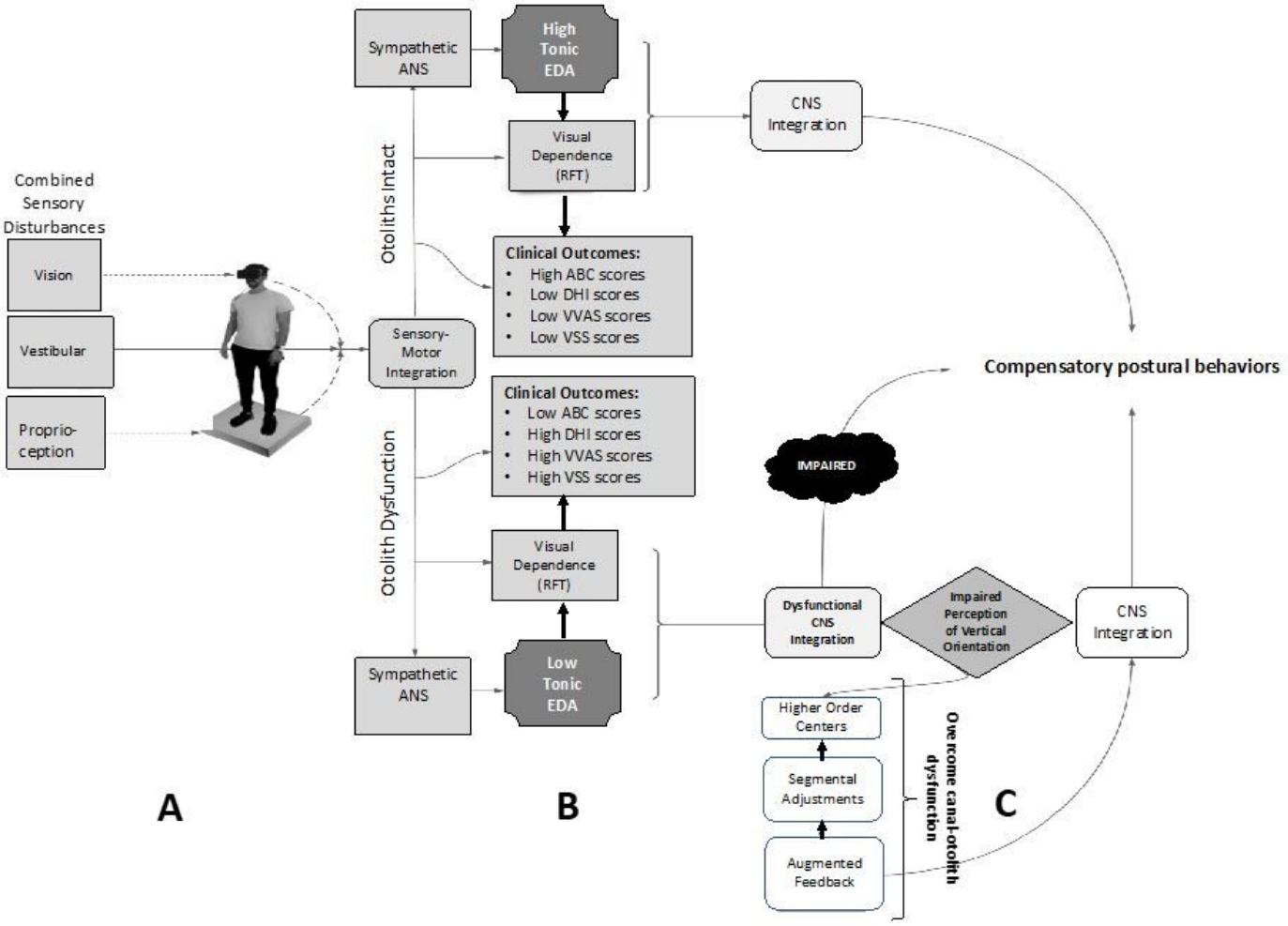

Figure 5

Conceptual schematic summarizing the results of this study and future recommendations for treatment of VVM. ***A.*** Visual, vestibular, and proprioceptive pathways were simultaneously disturbed during the experimental protocol, thereby modifying the sensory-motor integration task. ***B.*** Results of both objective (EDA) and subjective (RFT and outcomes) measures revealed distinct differences between the +VVM and -VVM groups, possibly indicative of dysfunction of the vestibular otoliths with +VVM. ***C.*** Impaired sensory processing in the CNS produces an impaired perception of vertical in the +VVM group, resulting in impaired compensatory postural behaviors. Potential interventions should focus on delivering augmented feedback to both segmental and higher order mechanisms in order to compensate for canal-otolith dysfunction. ***Abbreviations:***

VVM=visual-vestibular mismatch; *CNS*=central nervous system; *ANS*=autonomic nervous system; *EDA*=electrodermal activity; *RFT*=Rod and Frame test; *ABC*=Activities of Balance Confidence scale; *DHI*=Dizziness Handicap Inventory; *VVAS*= Visual Vertigo Analog Scale; *VSS*=Vertigo Symptoms Scale.