Title: Vestibular Rehabilitation Therapy for the Treatment of Vestibular Migraine, and the Impact of Post-Traumatic Brain Injury on Outcome: A Retrospective study. Authors: Stancel-Lewis, Jack¹, MSc.; Lau, Joanne^{1,2}, MBBS.; Male, Amanda³, MRes (Clin Prac).; Korres, George², M.D., Ph.D.; Rogel-Salazar, Jesus^{4,5}, Ph.D.; Pavlou, Marousa⁶, Ph.D.; Bamiou, Doris-Eva*1,2,7, M.D., Ph.D. 1. The Ear Institute, Faculty of Brain Sciences, University College London, London, UK 2. Neuro-Otology Department, University College London Hospitals, London, UK 3. Neurological Outpatient Physiotherapy Service, The National Hospital for Neurology and Neurosurgery, University College London Hospitals, London, UK 4. Faculty of Natural Sciences, Department of Physics, Imperial College London, UK 5. School of Physics, Engineering and Computer Science, Department of Physics, University of Hertfordshire, UK 6. Faculty of Life Sciences & Medicine, Kings College London, UK 7. Biomedical Research Centre, National Institute for Health Research, London, UK *Corresponding Author Professor Doris-Eva Bamiou M.D., Ph.D. d.bamiou@ucl.ac.uk Key Words: Vestibular Migraine, Migraine, Vertigo, Dizziness, Vestibular Rehabilitation Therapy, Traumatic Brain Injury, Head Trauma, Concussion. Conflicts of Interest and Source of Funding: None declared

Abstract

Introduction

Vestibular migraine (VM) is a common condition; individuals experience dizziness with migraine symptoms. Vestibular rehabilitation therapy (VRT) has been reported as an effective treatment for VM, however, evidence is limited. VM and traumatic brain injury (TBI) can co-occur, and some suggest that TBI can induce VM. There is limited evidence on the effect a history of TBI has on VRT in patients with VM.

Methods

Retrospective case series of 93 (f= 63, m= 30) participants who had VM and underwent VRT (mean age 48.62; SD15.92). Pre-treatment and posttreatment self-reported outcome measures and functional gait assessment were extracted from the participants health records and evaluated. The impact of TBI on VRT outcome in participants with VM was analysed. Individuals with TBI and no history of migraine (n=40) were also extracted to act as a control.

Results

VRT significantly improved self-reported dizziness on the Dizziness Handicap Inventory (DHI), with a mean change of -18 points (p <0.000) and +5 points on the Functional Gait Assessment (FGA) (p<0.000) in patients with VM. A history of TBI significantly impacted outcome on the DHI (p= 0.018) in patients with VM.

VRT significantly improved all outcome measures for individuals with TBI, with a mean change of -16 points on the DHI (p= 0.00) and +5 points on the FGA (p<0.000). The presence of VM significantly impacted outcome.

Conclusion

VRT should be considered as a treatment option to reduce dizziness and the risk of falls in individuals with VM. TBI may negatively impact VRT outcomes in individuals with VM.

112113 Introduction

Vestibular migraine (VM) is one of the most common vestibular disorders, affecting up to 1% of the general population (1). Clinical and diagnostic features include recurrent vertigo lasting 5 minutes to 3 days, associated with headache or migraine features \geq 50% of the time. Patients may report spontaneous, positional, visually induced and/or head-motion induced dizziness or vertigo. These symptoms may be accompanied by migraine-type headache, nausea, phono- and photophobia and/or visual aura (2).

Exercise based treatment programmes widely known as vestibular rehabilitation therapy (VRT) that incorporate multisensory components, including vestibular, vision and proprioception are acknowledged to improve symptoms of imbalance and vertigo in individuals with peripheral vestibular disorders (4). There is growing evidence that VRT is effective at improving dizziness, postural and gait stability, visual vertigo/visually induced dizziness and headache in individuals with VM (5, 6). Vitlovic et al (7) assessed the efficacy of a 6-month VRT programme in patients with VM compared to patients with vestibular impairment (VI) and no history of migraine. They found that the VM group experienced the same degree of benefit from VRT as the VI group. A more recent systematic review, evaluated the effects of VRT in the management of VM, which suggested VRT was effective in treating vertiginous symptoms in patients (8), although the available evidence was of low quality.

TBI results in a sequalae of symptoms which include dizziness and headache among others (9). VRT has been shown to be effective in improving dizziness, gait and postural stability following TBI (10-24). VM and TBI can co-occur, and some suggest that head trauma can induce vestibular migraine (12), however, there is deliberation about whether trauma induced migraine are true migraine, or migraine-like headaches resulting from a different pathological process (25). While the effectiveness of VRT in TBI populations without migraine has been widely reported, evidence of the association and interplay between TBI with VM symptoms and VM without TBI is limited.

Therefore, this study aims to add to the literature on the effect of the VRT on VM, look at the effect TBI has on the outcome of VRT in patients with VM and compare treatment outcomes in individuals with TBI and VM and those without.

Research Questions

- 1. Does VRT improve self-reported dizziness and functional gait in individuals with VM?
- 2. Does a history of TBI impact VRT outcome in individuals with VM?
- 3. Does VM impact VRT outcome in individuals with TBI?

Materials and Methods

Study design

A retrospective clinical service evaluation of the University College London Hospital (UCLH) electronic patient records. The clinical service evaluation was reviewed and authorised by the UCH Royal National Throat, Nose and Ear Hospital (RNHNEH) quality and safety manager on 10-05-2019. Risk of selection bias associated with a lack of randomisation, was accounted for by implementing consecutive series sampling.

Participants

162 Vestibular Migraine (VM) Group

Individuals aged ≥16 with a diagnosis of vestibular migraine made by UCH Audiovestibular Physician or Queen Square Neurologist, subsequently referred to Queen Square Neurological Outpatient

Physiotherapy Team for VRT between 2016 and 2018. Vestibular migraine was diagnosed as per the Barany Society and International Classification of Headache Disorders (ICHD) diagnostic criteria (2).

168169 Inc.

Inclusion criteria:

170171

172

173

166

167

- VM diagnosed according to established criteria (2)
- Pre- and post- VRT outcome measures
- Migraine under appropriate management before starting VRT programme
- >16 years of age

174 175

Traumatic Brain Injury (TBItotal) Group

176177178

179

180

181

182

183

184

The post traumatic dizziness population (TBItotal) included individuals aged ≥16 years who suffered a traumatic brain injury (TBI) and reported post-traumatic dizziness as a prominent symptom referred to UCH Audiovestibular Physician or Queen Square Neurologist and was then subsequently referred to Queen Square Neurological Outpatient Physiotherapy Team between 2010 and 2018. All patients seen during this period, including those with diagnosed VM were included in this study to reduce the possibility of selection bias. Those identified as having a history of VM were also included in the VM group. The Mayo TBI classification criteria and subclassifications as reported by Malec et al. (26) was used to define the severity of TBI.

185 186 187

Inclusion criteria:

188 189

190

191 192

193

194

195

196

- Clear history of TBI
- Pre- and post VRT outcome measures complete
- Duration between onset of dizziness and date of TBI < 12 months
- ≥16 years of age

Note: We wanted to include cases with dizziness that start/are reported immediately or shortly after the TBI – possible due to direct labyrinthine trauma- but were also mindful that possible causes of dizziness after TBI include diffuse axonal injury (Fife, Kalra Annals of New York Academy of Sience 2015), while axonal degeneration following TBI may continue for several years (

- 197 Axonal pathology in traumatic brain injury.
- Johnson VE, Stewart W, Smith DH.Exp Neurol. 2013 Aug;246:35-43.
-) and just over half of vestibular disorders post TBI will have a delayed onset (Characterisation and
 objective monitoring of balance disorders following head trauma, using videonystagmography.
- Naguib MB, Madian Y, Refaat M, Mohsen O, El Tabakh M, Abo-Setta A.J Laryngol Otol. 2012
 Jan;126(1):26-33.
 -). We thus made an operational decision to choose a 12 month window from the time of TBI to the onset of dizziness for the purposes of inclusion criteria.

204205206

203

Intervention

207208209

210

211

Participants were prescribed an individualised home exercise programme (HEP) including exercises that promoted gaze stabilisation, postural control and visual desensitization/habituation exercises. Participants were followed up in clinic as many times as deemed necessary by the highly specialised physiotherapists. Participants completed outcome measures prior to starting their exercise programme and at discharge.

212213

Outcome Measures

214215

Dizziness handicap inventory (DHI):

216217

The DHI is a 25-item questionnaire which measures the patient's self-perceived handicap related to dizziness, and self-perceived impact on the patient's quality of life in three domains: physical,

functional and emotional. The questionnaire provides a total score of 100, and the greater the score is, the higher the perceived impact the patient's symptoms are having on their quality of life. This questionnaire was chosen as it has been validated (27), has high test - re-test and internal reliability and is widely used in clinics and research to measure improvement in symptoms associated with VRT. A minimally clinically important change would be 18 points between pre- and post- treatment (95% CI) for the intervention to have had a significant change in self-perceived handicap (27). Scores of 0-30 would be considered mild, 31-60 as moderate and 61-100 as severe.

Visual Analogue Scale (VAS):

Visual analogue scales (VAS) are used to measure subjective characteristics or attitudes and changes in symptoms or attitudes in medical studies. The test is formed of either a 100 mm or 10 mm line, with interval numbers allowing the participant to judge the distance between the 2 extremes. The 10-point scale VAS is utilised for our study to self-report dizziness symptom severity (VAS Severity) and impact on quality-of-life from 0 (no symptoms) to 10 (the most severe) (VAS Impact). A change of VAS pain of 1.3 on a 10 point scale was identified as clinically significant in a trauma population (28), as well as in a more heterogenic population by Gallagher, Liebman (29). This study thus used a change of 1.3 as the minimum clinically significant change.

Functional Gait Assessment (FGA):

Functional Gait Assessment (FGA) is a 10-item assessment of postural stability during walking and simultaneously performing various motor tasks. Each item is scored from 0 to 3. High scores indicate better function, while lower scores indicate greater handicap. A score of 22 or lower would indicate a risk of falls. The FGA has a moderate correlation with the DHI (r=-0.64). The FGA has a high intrarater reliability in individuals with peripheral-vestibular disorders, with a high intraclass correlation coefficient (ICC =0.94) (30). The FGA shows excellent test-re-test reliability for individuals with stroke and Parkinson's disease (31); however, this is yet to be established for individuals with TBI. Internal consistency is excellent with a Cronbach alpha of 0.79 for vestibular disorders (32). A significant minimally detectable change is 6 points for vestibular disorders and clinically significant difference is 5 points in stroke.

Data-Collection Procedure

All patients who were diagnosed with VM or had a history of TBI and subsequently underwent VRT details were retrieved from the Neurorehabilitation Department at Queen Square, UCLH. Hospital numbers were used to search patient's electronic hospital record system (EHRS) using the Clinical Data Repository (CDR) and EPIC platforms. Clinic letters were manually retrieved to identify age, gender, diagnosis, number of follow ups, pre- and post-VRT outcome measures for all participants and for individuals with TBI, information to classify the severity of their TBI. Outcomes were recorded from the initial course of VRT following diagnosis of VM or from an initial course of VRT following TBI. Paper notes were requested for individuals with missing data.

Data clinics were held by two of the authors [JSL and JL]. Data was initially checked, in a blinded fashion and compared between the 2 authors. Any variability in interpretation of the data collected was discussed and a consensus agreed upon, with input by the senior author (this occurred 5 times in total). This cross-check process ensured the validity of the data collected.

Analysis

A result was considered statistically significant if the p value was ≤ 0.05 . All statistical analysis and descriptive statistics were performed using IBM SPSS Statistics version 25. To compare the main effect of treatment (for VM group regardless of TBI status and TBI total group regardless of VM status), appropriate repeated measure and paired samples statistical analysis was caried out. Parametric or non-

parametric tests were performed based on the normality of the distributions and assumptions required; tests included paired samples t-test and Wilcoxon Signed Rank.

Point-Biserial correlation analysis were carried out to assess whether there was an association between the presence of TBI and outcome using outcome measure change scores. ANCOVA was then performed if a significant corelation was identified between the presence of a TBI and outcome in the VM group to understand whether there was a significant impact on treatment outcome or not. Similar analyses were performed to understand if the presence of migraine in the TBI population had an impact on treatment outcome.

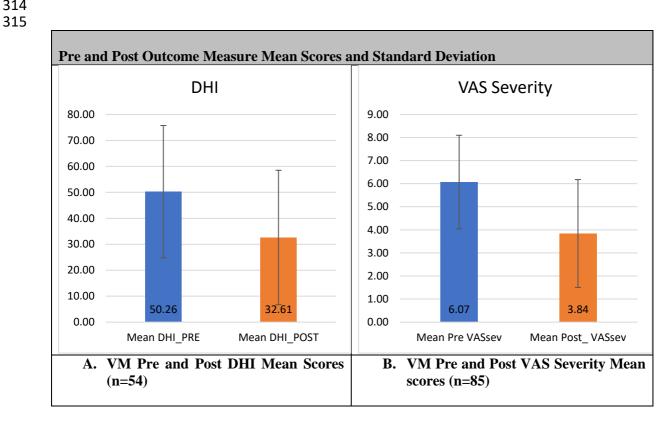
Univariate ANOVA was carried out to assess differences in baseline DHI scores between TBI Mayo subclassifications in the whole TBItotal group, and Chi-Squared analysis in the TBItotal group for those who had both pre- and post DHI scores.

Results

The population was formed of 93 (f= 63, m= 30) individuals diagnosed with VM, by an Audiovestibular Physician or Neurologist at UCLH Queen Square, who underwent a programme of VRT, with an average of 4 follow up sessions. Please see Table 1 for demographic information and outcomes measure mean change scores. Figure 2. Depicts the baseline and discharge mean outcome data.

Table 1. VM group Demographic and Mean Change Data. List of abbreviations: n= number; f= female; m= male; SD = standard deviation; TBI = traumatic brain injury; DHI = Dizziness Handicap Inventory; VASsev= ; VASimp=; FGA=

| Outcome | Vestibular Migraine Group |
|--|---|
| n (f / m) | N= 93 (63/30) |
| Age: mean (SD) | 48.62 (15.920) |
| Age Range: Min-Max | 16 - 89 |
| No. of follow Ups: mean (SD) | 3.75 (2.0229) |
| Treatment Duration Weeks: Median (Inter Quartile Range) | 29 (27) (TBI: 28.00 (18), No_TBI: 29.50 (30)) |
| Change DHI: N, mean (SD) | N=54, -17.65 (20.30) |
| Change VASsev: N, mean(SD) | N=85, -2.23 (2.20) |
| Change VASimp: N, mean(SD) | N=83, -2.21 (2.57) |
| Change FGA: N, mean(SD) | N=72, 4.88 (5.004) |



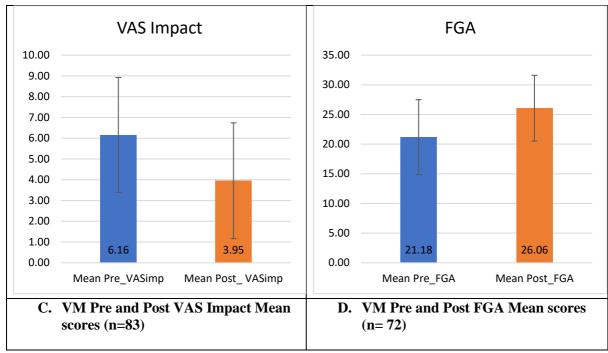


Figure 1.VM Group Mean Baseline and Discharge Outcome Data

Main effect- VM Group

 A paired samples t-test identified statistically significant main effect of treatment on the DHI (t (53) = 6.390, p <0.000, d = 0.870) with a mean improvement of -18 (20.30) points between pre and post scores. A statistically significant main effect of treatment was also identified on the VAS Severity scale (t (84) = 9.329, p <0.000, d = 1.012) and on the VAS Impact scale (t (82) = 7.831, p <0.000, d = 0.860) with a mean reduction in severity of symptoms of -2 (2.22) and a mean reduction in the impact of symptoms by -2 (2.56) points.

A Wilcoxon signed rank test identified a significant improvement in FGA scores following treatment (Z=-7.375, p<0.000), with a mean change of 5 (5.00) points.

Impact of TBI

A point-biserial correlation was run to determine if there was a relationship between the presence of TBI and DHI change scores. A moderate negative correlation between a history of TBI and change in DHI score was identified (r_{pb} =-0.314), which was statistically significant (p = 0.022,). There was no correlation between change scores and a history of TBI in any other measure see Table 2.

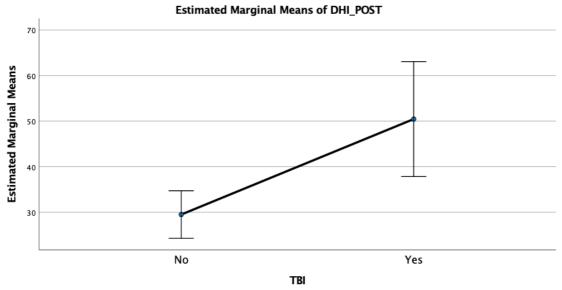
Table 2. VM Group, TBI Correlation Analysis . List of abbreviations

| Outcome | N (VM/VM_TBI) | correlation | Statistic |
|----------------------|---------------|-------------------------|-----------|
| Change DHI: | 53 (45/8) | r _{pb} =-0.314 | p = 0.022 |
| Change VAS Severity: | 85 (73/12) | $r_{pb} = -0.114$ | p = 0.571 |
| Change VAS Impact: | 83 (72/11) | r _{pb} =-0.092 | p = 0.410 |

| Change FGA: | 72 (64/8) | $r_{pb} = -0.009$ | p = 0.941 |
|-------------|-----------|-------------------|-----------|

Individuals who had VM and no history of TBI had a mean improvement of -20 (20.502) points on the DHI, whereas individuals with a history of TBI had a mean change of -3.00 (11.364). An ANCOVA was performed to determine the effect a history of TBI had on VRT outcome in individuals with VM. After adjustment for pre-test DHI scores, there was a statistically significant difference in post-test DHI score between the two groups (F(1,51)= 9.434,p=0.003).

Post-hoc analysis (Bonferroni corrected) identified that the presence of TBI resulted in significantly worse (p=0.003) post treatment scores compared to those without a history of TBI. This suggests that a history of TBI is a negative prognostic indicator for VRT in individuals with VM, and therefore a greater perceived handicap following VRT.



Covariates appearing in the model are evaluated at the following values: DHI_PRE = 50.26 Error bars: 95% CI

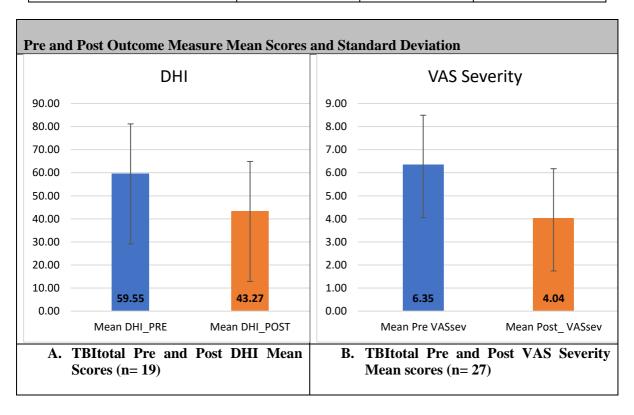
Figure 2. VM Group discharge DHI marginal means between those with TBI (yes) and those without (0).

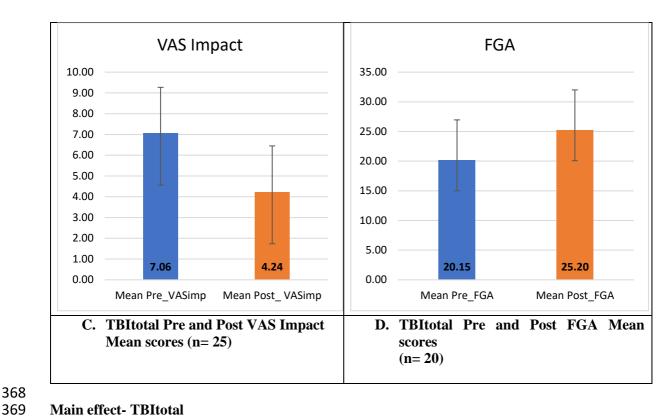
TBI control group

 The TBI population contained 60 participants, including individuals from the VM group (F=30, M=30) who met the inclusion criteria, with a mean age of 46 (range 16 to 78 years). Of these 60 individuals, 20 (f=10, m=10) had a history of VM from our main treatment group (referred to as the TBImigraine group). Table 1. Displays the demographic and mean change scores for each outcome measure and group.

Table 3. TBItotal group Demographic and Mean Change Data . List of abbreviations

| n (f / m) | N=60 (29/31) | N= 20 (10/10) | 40 (19/21) |
|----------------------------|-------------------------|--------------------|----------------------|
| Age: mean (SD) | 45.7 (15.148) | 40.0 (13.298) | 48.6 (15.35) |
| Age Range: Min-Max | 16-78 | 16-68 | 24-78 |
| HADs: n, mean total (SD) | N=19, 17.84(6.56)) | N=6, 20.83 (3.76) | N=13, 16.46 (7.22) |
| Change DHI: N, mean (SD) | N=22, - 16.27(20.18) | N=8, -3.00 (11.36) | N=14, -23.86 (20.45) |
| Change VASsev: N, mean(SD) | N=27, -2.31(2,57) | N=12, -1.88 (2.52) | N=15, -2.67 (2.637) |
| Change VASimp: N, mean(SD) | N=25, -2.82(2.30) | N=11, -2.82 (2.52) | N=14, -2.87 (2.18) |
| Change FGA: N, mean(SD) | N=20, 5.05(3.859) | N=8, 4.75 (4.20) | N=12, 5.25 (3.793) |





Main effect- TBItotal

370 371

372

373

374

375

376

377

378

379 380

381 382

383

384

385

386

387

388 389 A significant main effect of treatment was identified for the DHI (t (21) = 3.782 ,p= 0.001, d= 0.806) with a mean change of -16 (20.18), VAS Severity (Z=-3.685, p<0.000), with a median change of -2.00, VAS Impact (t(24) = 6.213, p<0.000) with a mean change of -2.84 (SD 2.29) and the Functional Gait Assessment (FGA) (t (-5.852) p<0.000) with a mean change of 5.05 (3.86). This indicates that dizziness following TBI improves with VRT. There was no significant difference in total Hospital Anxiety and Depression Scale (HADS) scores between the TBI and TBImigraine groups (F (1,17) = 1.916, p= 0.184), or between the groups (TBI and TBImigraine) in those who completed both pre- and post DHI scores (F (1,7) = 0.119, p= 0.741).

Correlation Analysis

We ran correlation analyses to decipher whether there was an association between the presence of migraine and outcome measure change scores. A point-biserial correlation was run to determine if there was a relationship between the presence of migraine and DHI change scores. A moderate negative correlation between the presence of migraine and the change in DHI score was identified (rpb=-0.509), which was statistically significant (p = 0.015,). There was no correlation between the presence of migraine and any other measure see Table 2.

Table 4. TBI Group, VM Correlation Analysis

| Outcome | N (TBImigraine/TBI) | correlation | Statistic |
|----------------------|---------------------|-------------------------|-----------|
| Change DHI: | 22 (8/14) | r _{pb} =-0.509 | p = 0.015 |
| Change VAS Severity: | 27 (12/15) | $r_s = -0.114$ | p = 0.571 |
| | | | |

| Change VAS Impact: | 25 (11/14) | r _{pb} =-0.001 | p = 0.997 |
|--------------------|------------|-------------------------|-----------|
| Change FGA: | 20 (8/12) | $r_{pb} = -0.065$ | p = 0.785 |

Dizziness Handicap Inventory (DHI)

Pre- and post-rehabilitation DHI scores were completed by 22 individuals in the TBItotal population with a mean score change of -16.27 (20.18). The TBItotal population was subdivided into individuals diagnosed with post-traumatic migraine (TBImigraine) and those that were not (TBI). The TBImigraine population (n=8) had a mean DHI score change of -3.00 (11.36) and the TBI population (n=14) had a mean DHI score change of -23.86 (20.45).

An ANCOVA was performed to determine whether the presence of migraine in a TBI cohort had a significant impact on VRT outcome. Following adjustments for the pre-rehabilitation DHI scores, a significant main effect of VRT between TBImigraine and TBI population post rehabilitation DHI scores was identified (F(1,19) = 6.67, p = 0.018).

Post-hoc analysis (Bonferroni corrected) identified that the TBI without migraine group's symptoms improved significantly more (p=0.018) than those with a history of TBI with migraine. This suggests that the presence of migraine has a significant, and negative impact on VRT outcome following TBI.

DHI accounting for sub classification

To ensure there was no differences in baseline scores between individuals with differing severity of TBI, analysis was carried out to assess differences in baseline mayo classification sub-groups. The "Symptomatic" mayo sub-group had a mean baseline DHI score of 52.83 (SD22.083), the "mild-probable" group had mean baseline score of 60.89 (SD 24.954) and the "moderate severe group" had a baseline mean of 56.35 (SD 26.151). There was no significant differences in base-line DHI scores between any of the Mayo classification level groups (F(2,52) = 0.395, p=0.676). There was also no significant difference between DHI change scores ($X^2(2)=0.784$, p=0.676) between all 3 subclassifications.

Discussion

Our study adds to the current literature that VRT is an appropriate and effective means of reducing self-reported dizziness and impaired functional gait in individuals with VM as reported by previous publications (8). Our VM population reported a clinically significant reduction in self-reported dizziness with a mean DHI score change of -18 points, a clinically significant reduction of severity and impact of symptoms reported on a VAS (-2 for both measures) and in functional gait assessed using the FGA when compared to neurological conditions such as stroke with a mean change of +5. The mean functional gait scores for our VM group improved from a population mean suggestive of being at risk of falls <22 to a population that was not.

Participants in our VM population had comparative baseline scores to other studies (5-7). Sugaya et al (6) reported a mean change in the DHI of -20 in their VM population following VRT programme, which is comparative to our VM group with a mean change of -20 when removing individuals with a history of TBI. However, a number of previous studies did not identify a clinically significant change in DHI self-report measures (5, 7).

We identified that a history of TBI in our VM population had a significant and negative impact of VRT outcome reported on the DHI. This indicates that a history of TBI could be a negative prognostic factor

for VRT in a VM population, however, the numbers within this subgroup were small and therefore should be interpreted with some degree of caution. Gottshall et al (13) assessed the effectiveness of VRT in "spontaneous migraine-associated dizziness" and "post-traumatic migraine-associated dizziness" VM in a population of individuals largely formed from active military personnel. Both the "spontaneous" and "post-traumatic" groups showed significant improvement in self-reported symptoms on the DHI (p<0.05), however, the "posttraumatic" group showed shorter symptom remission. Our study therefore contradicts these findings.

The differences in outcome between the VM group with and without a history of TBI may arise from different pathological processes and therefore respond to treatment differently. VM pathophysiology is not fully understood, however, activation of the trigeminal-vestibulocochlear reflex, resulting in neurogenic inflammation is believed to be a possible contributor to the symptoms experienced during an episode (34). Migraine following TBI results from a similar, but fundamentally different pathophysiological process by which neuroinflammation, cortical spreading depolarization and glutamate excitotoxicity plays a role, as well as diffuse axonal injury in functional regions of the brain (35).

It has been suggested previously that medication may help control visually induced symptoms in individuals with VM enabling them to better tolerate exercises (33). It was a requirement that the patient's migraine was managed before starting a VRT programme. However, as this was a retrospective study, we did not control for degree of symptom improvement by medication, type of medication or medication dose. Vitkovic et al (7) suggested that improvements in VM were noted regardless of medication regime. Future studies should look to control for migraine medication related factors, to understand the most appropriate pre-requisites for referral for VRT in patients with VM and what the degree of improvement conveyed by the VRT in stable cases.

Our study identified that VRT is effective at treating symptoms of post-traumatic dizziness, in line with current evidence which suggests an improvement in dizziness, gait and postural stability (10-24). Our TBI group included individuals with all TBI severity classification levels, whereas the majority of previous studies just report findings for mild to moderate individuals. We found that TBI classification did not impact outcome or baseline measures. Our TBI group had a clinically significant improvement in mean VAS severity and VAS impact scores (>1.3 points) and FGA (+5) showed clinically significant change in comparison to other neurological condition (significant \geq +5). The mean change in DHI scores from the TBItotal population (-16) fell short of what would be considered clinically significant (\geq -18), however, when assessing the subgroups within this study (TBI and TBImigraine) separately the mean DHI score change in the TBI subgroup (without a history of VM) (-24 points) would be considered clinically significant. There was no significant differences in HADS scores between the two TBI subgroups, therefore, this indicates that psychological profiles between those in the TBImigraine and TBI group were similar. These findings are consistent with Alsalaheen et al (17) who reported a mean 20-point reduction on the DHI.

Hoffer et al. (12) performed a prospective patient registry study in 58 individuals who had suffered a TBI and received VRT, that included 22 (41%) individuals with post-traumatic VM (PTVM). On average, the PTVM group returned to work sooner and reported baseline normal symptoms on self-reported measures compared to those without migraine subcomponent. This outcome is therefore different to our findings. The individuals in the TBI group had significantly improved DHI scores compared to those who had VM and a history of TBI. Similarly to the Gottshall et al (13) study, Hoffer et al (12) study was formed mainly of active or retired military personnel, which may result in a level of bias as individuals may have had higher baseline levels of fitness than average, may be more motivated to return to work and therefore more likely to report better outcomes in self-report measures or have different psychological profiles (36). Military personnel may be exposed to higher proportion of blast exposure than the civilian population, which poses a different mechanism than blunt head trauma and therefore potentially results different pathological process (37). This may indicate that our population is more generalisable. The TBI population with a history of VM fell greatly short of clinical significance on the DHI, with a reduction in mean score of -3 indicating that VM may negatively impact VRT outcome in individuals with TBI. This therefore may suggest that VM and migraine-like headaches

in individuals with a history of TBI and dizziness may result in poorer outcomes in individuals undergoing VRT.

Limitations

495

496

497 498

499 500

501

502

503

504

505

506

507

508

509

510511512

513514

515

516

517

518

519 520 521

522

Due to the retrospective nature of this study, the study was limited by missing data, lack of a headache specific measure and no clear control group to account for natural recovery with time or medication regime. We made an operational decision to include post-TBI dizziness with onset less than 12 months after the TBI, as more than half of post TBI vestibular disorders will have a delayed onset (ref), and vestibular disorders unrelated to TBI may have been included. Future studies should address these limitations and include randomised control trials to assess the impact of natural recovery, medication and combination treatments. Our group of VM with a history of TBI had limited numbers of individuals who completed both pre and post DHI outcome measures, therefore, results comparing to individuals with VM and history of TBI should be interpreted with caution as these small numbers may result in a large bias.

Conclusion

VRT can effectively manage self-reported dizziness and functional gait in individuals with VM. TBI may be a negative prognostic factor in individuals with VM undergoing VRT. Dizziness as a result of TBI can be effectively managed with personalized vestibular exercises, however, the presence of migraine may significantly impact outcome. However, the effect of time and medication regime was not assessed during this study and therefore results should be interpreted with cautious optimism.

References

- 523 1. Neuhauser HK, Radtke A, von Brevern M, Feldmann M, Lezius F, Ziese T, et al.
- Migrainous vertigo: prevalence and impact on quality of life. Neurology. 2006;67(6):1028-33.
- 526 2. Lempert T, Olesen J, Furman J, Waterston J, Seemungal B, Carey J, et al. Vestibular 527 migraine: diagnostic criteria. Journal of vestibular research: equilibrium & orientation.
- 528 2012;22(4):167-72.
- 529 3. Furman JM, Marcus DA, Balaban CD. Vestibular migraine: clinical aspects and pathophysiology. Lancet Neurol. 2013;12(7):706-15.
- 531 4. McDonnell MN, Hillier SL. Vestibular rehabilitation for unilateral peripheral
- vestibular dysfunction. The Cochrane database of systematic reviews. 2015;1:Cd005397.
- 533 5. Wrisley DM, Whitney SL, Furman JM. Vestibular rehabilitation outcomes in patients
- with a history of migraine. Otology & neurotology : official publication of the American
- Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 2002;23(4):483-7.
- 537 6. Sugaya N, Arai M, Goto F. Is the Headache in Patients with Vestibular Migraine 538 Attenuated by Vestibular Rehabilitation? Front Neurol. 2017;8:124.
- 7. Vitkovic J, Winoto A, Rance G, Dowell R, Paine M. Vestibular rehabilitation outcomes in patients with and without vestibular migraine. Journal of neurology. 2013;260(12):3039-48.
- 542 8. Alghadir AH, Anwer S. Effects of Vestibular Rehabilitation in the Management of a 543 Vestibular Migraine: A Review. Frontiers in neurology. 2018;9:440-.
- 544 9. Sandel N, Collins MW. Diagnosis and Management of Mild Traumatic Brain Injury.
- 545 Current Trauma Reports. 2018:1-11.

- 546 10. Gurr B, Moffat N. Psychological consequences of vertigo and the effectiveness of
- vestibular rehabilitation for brain injury patients. Brain injury. 2001;15(5):387-400.
- 548 11. Marzo SJ, Leonetti JP, Raffin MJ, Letarte P. Diagnosis and management of post-
- traumatic vertigo. The Laryngoscope. 2004;114(10):1720-3.
- 550 12. Hoffer ME, Gottshall KR, Moore R, Balough BJ, Wester D. Characterizing and treating
- 551 dizziness after mild head trauma. Otology & neurotology: official publication of the
- 552 American Otological Society, American Neurotology Society [and] European Academy of
- 553 Otology and Neurotology. 2004;25(2):135-8.
- 554 13. Gottshall KR, Moore RJ, Hoffer ME. Vestibular rehabilitation for migraine-associated
- 555 dizziness. Int Tinnitus J. 2005;11(1):81-4.
- 556 14. Hoffer ME, Balough BJ, Gottshall KR. Posttraumatic balance disorders. Int Tinnitus J.
- 557 2007;13(1):69-72.
- 558 15. Brown KE, Whitney SL, Marchetti GF, Wrisley DM, Furman JM. Physical therapy for
- central vestibular dysfunction. Archives of physical medicine and rehabilitation.
- 560 2006;87(1):76-81.
- 561 16. Gottshall KR, Hoffer ME. Tracking Recovery of Vestibular Function in Individuals With
- 562 Blast-Induced Head Trauma Using Vestibular-Visual-Cognitive Interaction Tests. Journal of
- Neurologic Physical Therapy. 2010;34(2):94-7.
- 17. Alsalaheen BA, Mucha A, Morris LO, Whitney SL, Furman JM, Camiolo-Reddy CE, et
- al. Vestibular rehabilitation for dizziness and balance disorders after concussion. Journal of
- neurologic physical therapy: JNPT. 2010;34(2):87-93.
- 567 18. Schneider K, Meeuwisse W, Nettel-Aguirre A, Boyd L, Barlow K, Emery C. Cervico-
- vestibular physiotherapy in the treatment of individuals with persistent symptoms following
- sport-related concussion: a randomized controlled trial. British Journal of Sports Medicine.
- 570 2014;48:1294-8.
- 571 19. Kleffelgaard I, Soberg HL, Bruusgaard KA, Tamber AL, Langhammer B. Vestibular
- 572 Rehabilitation After Traumatic Brain Injury: Case Series. Physical therapy. 2016;96(6):839-
- 573 49.
- 574 20. Moore BM, Adams JT, Barakatt E. Outcomes Following a Vestibular Rehabilitation
- and Aerobic Training Program to Address Persistent Post-Concussion Symptoms. Journal of
- 576 allied health. 2016;45(4):e59-e68.
- 577 21. Reneker JC, Hassen A, Phillips RS, Moughiman MC, Donaldson M, Moughiman J.
- 578 Feasibility of early physical therapy for dizziness after a sports-related concussion: A
- 579 randomized clinical trial. Scandinavian Journal of Medicine & Science in Sports.
- 580 2017;27(12):2009-18.
- 581 22. Kontos AP, Collins MW, Holland CL, Reeves VL, Edelman K, Benso S, et al. Preliminary
- 582 Evidence for Improvement in Symptoms, Cognitive, Vestibular, and Oculomotor Outcomes
- 583 Following Targeted Intervention with Chronic mTBI Patients. Military Medicine.
- 584 2018;183(suppl_1):333-8.
- 585 23. Jafarzadeh S, Pourbakht A, Bahrami E, Jalaie S, Bayat A. Effect of Early Vestibular
- 586 Rehabilitation on Vertigo and Unsteadiness in Patients with Acute and Sub-Acute Head
- 587 Trauma. Iranian journal of otorhinolaryngology. 2018;30(97):85-90.
- 588 24. Kleffelgaard I, Soberg HL, Tamber A-L, Bruusgaard KA, Pripp AH, Sandhaug M, et al.
- The effects of vestibular rehabilitation on dizziness and balance problems in patients after
- traumatic brain injury: a randomized controlled trial. Clinical Rehabilitation. 2018;33(1):74-
- 591 84.

- 592 25. Labastida-Ramírez A, Benemei S, Albanese M, D'Amico A, Grillo G, Grosu O, et al.
- 593 Persistent post-traumatic headache: a migrainous loop or not? The clinical evidence. The
- 594 Journal of Headache and Pain. 2020;21(1):55.
- 595 26. Malec JF, Brown AW, Leibson CL, Flaada JT, Mandrekar JN, Diehl NN, et al. The mayo
- 596 classification system for traumatic brain injury severity. Journal of neurotrauma.
- 597 2007;24(9):1417-24.
- 598 27. Jacobson GP, Newman CW. The development of the Dizziness Handicap Inventory.
- 599 Archives of otolaryngology--head & neck surgery. 1990;116(4):424-7.
- 600 28. Todd KH, Funk KG, Funk JP, Bonacci R. Clinical Significance of Reported Changes in
- Pain Severity. Annals of Emergency Medicine. 1996;27(4):485-9.
- 602 29. Gallagher EJ, Liebman M, Bijur PE. Prospective validation of clinically important
- changes in pain severity measured on a visual analog scale. Annals of Emergency Medicine.
- 604 2001;38(6):633-8.
- 605 30. Nilsagård Y, Kollén L, Axelsson H, Bjerlemo B, Forsberg A. Functional gait assessment:
- Reliability and validity in people with peripheral vestibular disorders. International Journal
- of Therapy and Rehabilitation. 2014;21(8):367-73.
- 408 31. Yang Y, Wang Y, Zhou Y, Chen C, Xing D. Reliability of functional gait assessment in
- patients with Parkinson disease: Interrater and intrarater reliability and internal consistency.
- 610 Medicine (Baltimore). 2016;95(34):e4545-e.
- 611 32. Wrisley DM, Marchetti GF, Kuharsky DK, Whitney SL. Reliability, Internal Consistency,
- and Validity of Data Obtained With the Functional Gait Assessment. Physical therapy.
- 613 2004;84(10):906-18.
- 614 33. Whitney SL, Wrisley DM, Brown KE, Furman JM. Physical therapy for migraine-
- related vestibulopathy and vestibular dysfunction with history of migraine. The
- 616 Laryngoscope. 2000;110(9):1528-34.
- 617 34. Espinosa-Sanchez JM, Lopez-Escamez JA. New insights into pathophysiology of
- vestibular migraine. Frontiers in neurology. 2015;6:12-.
- 619 35. Mares C, Dagher JH, Harissi-Dagher M. Narrative Review of the Pathophysiology of
- 620 Headaches and Photosensitivity in Mild Traumatic Brain Injury and Concussion. The
- 621 Canadian journal of neurological sciences Le journal canadien des sciences neurologiques.
- 622 2019;46(1):14-22.

- 623 36. Xue C, Ge Y, Tang B, Liu Y, Kang P, Wang M, et al. A meta-analysis of risk factors for
- 624 combat-related PTSD among military personnel and veterans. PloS one.
- 625 2015;10(3):e0120270.
- 626 37. Hoffer ME, Donaldson C, Gottshall KR, Balaban C, Balough BJ. Blunt and blast head
- trauma: different entities. Int Tinnitus J. 2009;15(2):115-8.