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1 **Neuropsychiatric Outcomes in UK Military Veterans with Mild Traumatic Brain Injury**
2 **and Vestibular Dysfunction**

3
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Abstract

Objective: To estimate the frequency of vestibular dysfunction following blunt, blast, and blunt & blast mild traumatic brain injury (mTBI) and thereon assess the long-term impact of vestibular dysfunction on neurobehavioral function and disability independently of co-morbid psychiatric symptoms. **Setting:** Combat Stress residential and Veterans' Outreach drop-in centres for psychological support. **Participants:** 162 help-seeking UK military veterans. **Main measures:** Self-reported frequency and severity of mTBI (using the Ohio State Identification Method), Vertigo Symptom Scale, PTSD checklist for DSM5, Kessler Psychological Distress Scale, Neurobehavioral Symptom Inventory, HIT6, Memory Complaints Inventory, WHO Disability Assessment Scale 2.0. **Results:** 72% of the sample reported one or more mTBI over their lifetime. Chi-square analyses indicated that vestibular disturbance, which affected 69% of participants, was equally prevalent following blunt (59%) or blast (47%) injury and most prevalent following blunt and blast combined (83%). Mediation analysis indicated that when PTSD, depression and anxiety were taken into account, vestibular dysfunction in participants with mTBI was directly and independently associated with increased postconcussive symptoms and functional disability. **Conclusion:** Vestibular dysfunction is common after combined blunt and blast mTBI and singularly predictive of poor long-term mental health. From a treatment perspective, vestibular rehabilitation may provide relief from postconcussive symptoms other than dizziness and imbalance. **Keywords:** *Balance, mTBI, blast, blunt, veterans.*

53 Introduction

54 Between the periods of 2003 to 2011 there were 2440 UK casualties in Operations Herrick
55 (Afghanistan) and TELIC (Iraq).¹ Approximately 19% of casualties sustained a traumatic
56 brain injury and although 87% were graded as moderate-to-severe, estimates derived from
57 US personnel give reason to believe that the incidence of mild TBI (mTBI) was likely
58 under-reported.² mTBI acquired during combat is significantly associated with long-term
59 neuro-behavioural and psychiatric (most notably PTSD) disturbance, and is a risk factor
60 for alcohol abuse and general disability. Elevated exposure to munitions explosions leave
61 military personnel uniquely susceptible to blast-induced mTBI which, perhaps
62 unsurprisingly, is associated with damage to the vestibular organs of the inner ear.
63 Vestibular injury can also be sustained through blunt injury to the back of the head via
64 projectile or fall. Of particular interest here, studies in civilians show overlap in the
65 neurobehavioural and psychiatric symptoms that accompany vestibular dysfunction and
66 mTBI. Coupled with the fact that vestibular assessment is not routinely performed on
67 military personnel, this raises the possibility that some symptoms which are vestibular in
68 origin have been misattributed to mTBI. In the present study, we compared the relative
69 prevalence of vestibular symptoms in blast and blunt mTBI in help-seeking UK veterans
70 to determine the group most at risk of vestibular-related impairment. We then determined
71 the contribution of vestibular dysfunction to neuropsychiatric function and more general
72 disability.

73 The estimated incidence of mTBI ranges between 15%³ and 23%⁴ in US personnel
74 to 3.2%⁵ and 13.5% in UK personnel.^{1,6} Several factors may help explain this discrepancy
75 including the greater reliance on self-report rather than medical records in the US, and the
76 shorter deployment periods of UK soldiers (6 months compared to 12-18 months for US

77 personnel). There is however an emerging consensus that the effects of mTBI sustained
78 during deployment are best understood within the context of lifetime TBI exposure.⁷

79 mTBI is associated with a broad range of psychiatric and neurological symptoms,
80 the most common of which are headache, fatigue, sleep disorder, dizziness, amnesia,
81 information processing slowing, executive dysfunction, depression and anxiety.⁸ mTBI
82 sustained in combat is often accompanied by PTSD and bodily trauma which can make it
83 difficult to determine the relative contribution of each of these factors. Studies indicate
84 that mTBI is not by itself a strong determinant of well-being and general functional
85 outcome in veterans.⁹ Rather, it becomes so when accompanied by co-morbid neurological
86 and psychiatric complications. For example, Lippa et al.,⁹ found that while combat
87 veterans with a history of mTBI reported more psychiatric and behavioural conditions,
88 their disability (as measured by the World Health Organisation Disability Assessment
89 Schedule II) was not significantly affected. By contrast, Lippa et al.,⁹ found that the
90 concurrence of mTBI with PTSD and depression afforded a unique vulnerability to poor
91 general outcome, causing a substantial worsening of independent function, self-care and
92 social reintegration.

93 Another common co-morbidity in military mTBI is vestibular impairment although
94 its effect on mental health is less clear. The vestibular system comprises peripheral organs
95 located within the labyrinth of the inner ear which detect angular and linear acceleration of
96 the head. These organs convey information via the brainstem vestibular nuclei to cortical
97 and sub-cortical regions involved in sensori-motor control, interoception and spatial
98 cognition. Although not as well characterised as audiological impairment, vestibular
99 impairment can be induced by the blast wave from a nearby munitions explosion which
100 induces an over-pressurisation followed by an under-pressurisation in the air and fluid
101 filled chambers of the inner ear.¹⁰ The mechanical damage caused by such a blast wave

102 can be compounded by noise-induced damage (typically >140dB), toxin exposure, and, if
103 the individual falls over and bangs the back of the head or is hit by a projectile, blunt
104 injury.¹¹ Aside from causing middle and inner ear damage, white matter abnormalities and
105 diffuse axonal injury have been observed in cerebellum, thalamus and ventral posterior
106 cerebral cortex in mTBI patients presenting with vestibulopathy.¹² The presence of these
107 abnormalities has been shown to correlate with time to recovery and neurocognitive test
108 performance. Unfortunately, vestibular symptoms are among the most common after
109 mTBI. In the large-scale study (n=907) conducted by Terrio et al,⁴ dizziness and balance
110 problems were the second most commonly reported symptom reported by individuals
111 immediately after sustaining mTBI, with 11.5% reporting persistent problems post-
112 deployment. In a case series, Hoffer et al.¹³ reported that 84% of mTBI veterans who had
113 sustained a blast-related mTBI had acute dizziness symptoms more than 30days after
114 injury.¹³ A follow-up study in a smaller cohort indicated persistent postural instability up
115 to 7 years later,¹⁴ a concerning finding given that dizziness at just 6 months post-onset is
116 closely linked to psychological distress and failure to return to work.¹⁵

117 A growing number of studies indicate that damage to the vestibular system affects
118 neuropsychiatric function in a manner quite similar to that found in postconcussive
119 syndrome. In a seminal paper, Grimm et al. reported cognitive disturbances in patients
120 diagnosed with perilymph fistula syndrome including general forgetfulness, a specific
121 deficit in auditory short-term memory, apraxia, and a general slowing of information
122 processing.¹⁶ Fatigue, anxiety, depression and unexplainable dread were also commonly
123 observed, and contributed to a clinical picture that the authors described as functionally
124 devastating. More recent study has shown similar symptoms in patients diagnosed with
125 vestibular migraine and other non-traumatic pathologies,¹⁷ while a large-scale survey of
126 20,950 adults in the US revealed that the 8% who self-reported vestibular vertigo were

127 eight times more likely to have serious difficulty concentrating or remembering, four
128 times more likely to have limitations on daily living, and three times more likely to suffer
129 from depression, anxiety or panic disorder.¹⁸

130 Veterans who show balance impairment, either via questionnaire¹⁹ or
131 vestibulography²⁰ are also much more likely to report PTSD symptoms, a finding that may
132 derive from the shared neurochemical features of the ascending vestibular afference and
133 limbic and arousal systems.²¹ This same network has also been implicated in the strong
134 association between balance impairment and migraine headache.²¹ More recently, Haber et
135 al,²⁰ reported high correlations in 30 veterans between balance/postural impairment and
136 self-reports of fatigue, depression and PTSD. Together these indicate that the disturbances
137 in gravitational and head-centred frames of reference induced by vestibular disorder
138 compromise brain processes not only involved in balance and autonomic motor control but
139 intellectual, emotional, interoceptive and arousal regulation too. Such indications raise the
140 possibility that vestibular impairment makes an independent contribution to the neuro-
141 behavioural and functional capacity of military veterans, regardless of whether mTBI has
142 been sustained.

143 The aims of the present study were two-fold. First, we sought to establish, for the
144 first time, the relative prevalence of chronic vestibular injury in veterans with either blunt,
145 blast or blunt+blast lifetime mTBI. Although each of these mechanisms of injury can
146 damage the vestibular system, there is uncertainty over which, if any, show the strongest
147 association and thereby constitute the greatest risk for vestibular-related impairment. By
148 means of comparison, studies of auditory dysfunction in military traumatic brain injury
149 show a stronger association with blast injury; 62% and 38% of combat veterans who had
150 sustained blast TBI reported hearing loss and reported tinnitus respectively, while only
151 44% and 18% of veterans in the non-blast group reported hearing loss and tinnitus

152 respectively.²² The second, and most important, study aim was to conduct an exploratory
153 investigation of the direct and indirect associations between vestibular symptoms and both
154 postconcussive symptoms and more general disability. Statistical mediation analysis was
155 applied to determine whether postconcussive symptoms and more general disability are
156 linked with vestibular symptoms independently of depression, anxiety and PTSD which
157 have also been shown to exert influence. Mediation analysis also made it possible to
158 examine the interplay between vestibular and psychiatric factors which in studies of UK
159 veterans has been hampered by the absence of standardised vestibular and neuro-
160 behavioural measures.

161 Study recruitment was restricted to veterans actively seeking psychological support
162 given their poor life outcomes and the higher likelihood of vestibular impairment in
163 individuals reporting psychiatric disturbance.

164

165 **Methods**

166 **Participants**

167 162 participants (158 White British, 4 Black British) were recruited for study - see Table I for
168 their demography and military background. 137 were recruited from a 6week programme of
169 in-patient psychiatric treatment at one of three *Combat Stress* treatment centres in the UK,
170 and 25 participants were recruited from drop-in counselling sessions at the *Portsmouth*
171 *Veterans Outreach* Centre. Individuals were eligible if over 18 years old, retired from the UK
172 armed forces, and willing to consent to study participation. Potentially eligible participants
173 were approached shortly after their treatment/counselling session and asked if they would be
174 willing to conduct a survey aimed at assessing military veterans' experience of head injury.
175 Favourable ethical opinions were given prior to study commencement from the University of
176 Kent School of Psychology and Combat Stress research ethics review panels.

177

178 Procedure

179 Following written informed consent, participants completed the survey in a quiet corner
180 room accompanied by the experimenter. The survey comprised a number of validated,
181 standardised self-report assessments presented serially using the on-line survey software
182 *Qualtrics* on an iPad. These assessments were administered in the order in which they
183 appear below and were preceded by questions about demographic background and
184 military service. Participants were told that they could take breaks throughout the survey
185 as needed.

186

187 Self-Report Measures

188 Participants' lifetime history of TBI was measured using The Ohio State TBI
189 Identification Method (OSTIM).²³ Additional questions were added from the Boston
190 Assessment of TBI-lifetime (BAT-L) to determine blast proximity.²⁴ Responses to the
191 OSTIM determined the presence/absence and severity of TBI using the US Department of
192 Defense and Department of Veterans Affairs screening definitions.²⁵ mTBI classification
193 involved an alteration of consciousness or mental state for a moment up-to 24hours post
194 injury, and/or a loss of consciousness (LOC) of 0 to 30minutes and/or a presence of post-
195 traumatic amnesia lasting less than one day. Moderate TBI was defined by a LOC for
196 more than 30minutes and less than 24hours. Severe TBI was categorized as a LOC lasting
197 more than 24hours. Vestibular symptoms were assessed using the Vertigo Symptom Scale
198 Long form (VSSL) which comprises 22 items that quantify the duration and severity of
199 vertigo and other dizziness symptoms.²⁶ Current postconcussive symptoms were mainly
200 assessed using the Neurobehavioral Symptom Inventory (NSI),²⁷ although the Headache
201 Impact Test (HIT6)²⁸ and Epworth Sleepiness Scale (ESS)²⁹ were also administered to

202 more comprehensively probe the predicted association between vestibular symptoms and
203 headache and daytime sleepiness. PTSD symptoms were assessed via the PTSD Checklist
204 for DSM-5 (PCL-5),³⁰ and depression and anxiety were assessed using the Kessler
205 Psychological Distress Scale (K10).³¹ Functional Disability was assessed using the World
206 Health Organisation Disability Assessment Schedule II short version (WHODAS 2.0).³²
207 Symptom exaggeration was assessed using the Memory Complaints Inventory (MCI)
208 which has been validated in military personnel with a history of concussion and in civilian
209 populations presenting with anxiety and depression.^{34,33}

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211
212

Results

213 Statistical Analyses

214 Summary statistics were calculated for the demographic, TBI and co-morbid characteristics
215 of the sample. Chi-square analyses were then applied to compare the relative frequency of
216 vestibular impairment in participants with self-endorsed blunt, blast, or blunt+blast (i.e. both
217 blunt and blast) mTBI. For the purpose of the chi-square analysis, participants who reported
218 dizziness symptoms more than 3 times per year were classified as suffering from vestibular
219 disturbance while those who reported symptoms either never or only 1-3 times per year were
220 classified as not suffering from vestibular disturbance. Mediation analyses³⁵ were conducted
221 on scores provided by those who self-endorsed mTBI to determine if the severity of their
222 vestibular symptoms (as measured by the VSSL total score) independently contributed to the
223 broad profile of postconcussive symptoms (as measured by the NSI and HIT6) and disability
224 (WHO-DAS 2.0) when depression, anxiety and PTSD were taken into account as mediators.
225 The mediation analysis was also used to interrogate the relationship between vestibular
226 symptoms and each of these mediators, and between these mediators and each of the outcome
227 variables (NSI, HIT6 and WHO-DAS 2.0). Finally, the analysis allowed us to assess the

228 combined association (i.e. total effect) of the predictor and mediator variables with the
229 outcome measures.

230 Post hoc exploratory analysis interrogated the statistical outcomes of the NSI
231 mediation analysis. A sensitivity analysis was conducted in which the mediation analysis
232 was re-run on the adjusted NSI total score scores after the 3 items (items 1-3) on the NSI
233 that relate to imbalance/unsteadiness were removed. This was carried out to determine if
234 the observed association partly reflects the fact that both questionnaires probe several
235 common symptoms. To estimate the extent to which the observed relationship between
236 VSSL and NSI scores reflect vertigo and balance factors as opposed to autonomic and
237 anxiety-related factors, two other modified versions of the original NSI mediation analysis
238 were run; the first replaced the VSSL total score with the VSSL vertigo-balance
239 subdomain score while the second replaced the VSSL total score with the autonomic-
240 anxiety subdomain score.

241 Participants with missing data were excluded from analysis. All inferential
242 analyses were computed using SPSS 24.

243

244 **Overview of Sample Characteristics**

245 Please see Table 1 for the sample demographic, Table 2 for participants' lifetime history and
246 prevalence of mTBI, and Table 3 for their co-morbid neuropsychiatric symptoms. The mean
247 age of the group, which was mostly male, was 46.6 years (standard deviation = 9.3) and had
248 been deployed to a war zone an average of 4 times. Seventy two percent of the sample
249 reported a lifetime history of one or more mTBIs (M age = 24.4, SD = 10.52), 74% of which
250 resulted in a visit to an A&E department or acute military medical facility. 49% reported that
251 they had periods in their lives where they had sustained repeated mTBIs. As shown in Table
252 3, the majority reported neuro-behavioural and neuro-psychiatric symptoms including

253 imbalance, headache, daytime sleepiness, PTSD, and depression/anxiety. The average
254 WHODAS score was 20.49 ($SD = 10.70$), which is worse than approximately 90% of the
255 general international population.³⁶ Seventy-three participants (50%) indicated that they drank
256 alcohol regularly, consuming a weekly average of 20.9 units (alcohol units defined by the UK
257 Department of Health)³⁷. Most of the sample ($n = 118$) had never used recreational drugs. 56
258 of the 110 participants with one or more mTBI who completed the MCI fell below the cut-off
259 score (<40%) for symptom exaggeration. The mean MCI score was 39.59 ($SD = 19.8$).

260 Tables 1 and 2 here

261

262 **Blast & Blunt mTBI**

263 Sports related mTBI (62%) was the most common method of blunt injury although
264 injuries sustained via road traffic accidents (49%) were also prevalent. The majority of the
265 mTBI sample (81%) indicated that they had been exposed to blast during their military
266 career. 50% sustained one or more blast mTBIs, and 53% of this sub-group reported 3 or
267 more blast mTBIs. Of these blast mTBIs, 38 were sustained within a proximity of 0-
268 10meters, 15 within 11-25 meters and 5 within 26-100 meters.

269 47% ($n=8$) of participants in the blast only category reported vestibular
270 disturbance, 59% ($n=35$) reported vestibular disturbance in the blunt only category, and
271 83% ($n=34$) reported vestibular disturbance in the blunt and blast category. Chi-square
272 analysis indicated a significant association between mechanism of injury and the presence
273 of vestibular disturbance $\chi^2(2) = 9.70, p = .008$. Interpretation of the 2x2 contingency
274 tables (using a bonferonni corrected alpha of 0.017) indicated no significant difference
275 between the observed frequencies of vestibular disturbance following blunt or blast ($\chi^2(1)$
276 $= 1.46, p = .223$). However, the frequency of vestibular disturbance was significantly

277 greater for blunt+blast compared to blast ($\chi^2(1) = 9.19, p = .006$) and marginally greater for
278 blunt+blast compared to blunt ($\chi^2(1) = 5.61, p = .018$).

279 Table 3 about here

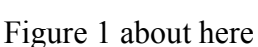
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281 **Mediation analyses**

282 Multiple linear regression was first conducted to identify which test variables listed in
283 Table 3 were statistically associated with vestibular impairment and could therefore be
284 included in the mediation analysis. This showed significant associations ($p < 0.01$) between
285 the severity of vestibular symptoms and all variables (coefficient scores ranged from 0.5 to
286 0.8) except sleepiness (see supplemental Tables 5, 6 and 7 for correlation matrices). Age
287 was also added to this regression but did not show a statistically significant association so
288 was not carried forward. Mediation analysis were then conducted using Hayes PROCESS
289 macro for SPSS³⁸, which bias-corrected the sample by bootstrapping a sample of 10,000
290 using 95% confidence intervals. Coefficients were considered statistically significant at p
291 $< .05$. Three mediation analysis were applied to determine if the severity of vestibular
292 disturbance, as defined by VSSL total score, imposed a direct effect on postconcussive
293 symptoms (NSI), headache (HIT6) and disability (WHODAS) independent of mediators
294 PTSD (PCL-5), depression and anxiety (K10).

295 As can be seen in Figure 1, the VSSL scores exerted a direct effect on the NSI
296 (Figure 1.1), HIT6 (Figure 1.2) and WHO-DAS 2.0 (Figure 1.3) scores independently of
297 the psychiatric mediators in all three mediation models. There was also a significant
298 association between VSSL score and the psychiatric mediators of depression, anxiety
299 (K10) and PTSD (PCL-5) (see a_1 and a_2 pathways in figures). As expected, depression and
300 anxiety were strongly associated with outcome in all three mediation models (see b_2 in
301 figures), although PTSD symptoms showed no significant influence (see b_1 in figures).

302 While VSSL scores directly affected NSI scores, they showed no effect when combined
303 with PTSD scores within the indirect pathway a_1*b_1 . By contrast, when combined with
304 the depression and anxiety scores within the indirect a_2*b_2 pathway, VSSL scores were
305 significantly associated with NSI scores. Finally, there were a significant total effect
306 across all three mediation analyses, indicating that vestibular symptoms were significantly
307 associated with outcome both independently and in conjunction with the psychiatric
308 mediators.

309 

310 **Exploratory Analysis**

311 Sensitivity analysis indicated that both the direct and indirect effects of VSSL scores on
312 the NSI remained significant after the 3 dizziness-related items on the NSI were removed
313 (see Table 4a.) Likewise, the pattern of statistical significance remained unchanged when
314 the mediation analysis was re-run after replacing the VSSL total scores with first the
315 VSSL vertigo subdomain scores and then the VSSL anxiety-related scores (see Table 4b).

316

317 

318

319 **Discussion**

320 This is the first study to systematically assess if vestibular impairment, both directly and in
321 conjunction with psychiatric co-morbidities, is associated with long-term postconcussive
322 symptoms and general disability in military veterans reporting a lifetime history of mTBI.
323 Seventy two percent reported one or more mTBI in their lifetime, a prevalence that is
324 almost identical to the 71% lifetime estimate for US veterans⁷ but higher than other UK
325 estimates which have focused on mTBI acquired during service or utilised less detailed
326 lifetime assessments. Approximately one half of those with mTBI reported periods in their

327 life when they sustained repeated injury. The most frequent mechanism of injury was
328 blunt mTBI, mainly acquired during sports activity and road traffic accident. 81% of the
329 mTBI sample indicated they had been exposed to blast, with 50% reporting mTBI as a
330 consequence. 53% of this subgroup reported blast mTBI on three or more occasions with
331 approximately two-thirds occurring within 10 meters of the explosion which is notable
332 given that such close exposure has been associated with decreased parietal-frontal
333 connectivity.³⁹ Three quarters of those who sustained an mTBI visited either an A&E
334 department or acute military medical facility. Over the longer-term, more than one half of
335 those who sustained mTBI reported persistent postconcussive neurobehavioural symptoms
336 including dizziness, headache and daytime sleepiness, as well as depression, anxiety, and
337 PTSD. Alcohol consumption exceeded current UK government guidelines of 14 units per
338 week,³⁷ and general disability fell within the bottom 10% of the general international
339 population.³⁶ Together these data highlight significant, long-term care needs in help-
340 seeking UK military veterans with a self-reported history of mTBI.

341 Consistent with the high prevalence reported in other military samples, 69%
342 reported symptoms consistent with a chronic vestibular disturbance. To our knowledge,
343 this is the first study to determine whether the likelihood of vestibular disturbance is
344 influenced by the manner in which mTBI is acquired. Chi-square analysis indicated that
345 vestibular disturbance was most commonly experienced following blunt and blast injury
346 combined rather than by only blunt or blast; 83% of blunt+blast mTBI reported vestibular
347 disturbance compared to 47% and 59% for blast and blunt respectively. This finding
348 contrasts with the predominance of blast injury in soldiers with auditory impairment and
349 may partly reflect the insulation afforded by the deep-lying, bony labyrinth to external
350 pressure waves. Although it is unclear how much the vestibular impairment sustained by
351 blunt and blast injury reflects peripheral as opposed to central nervous damage, its high

352 prevalence suggests that this blunt and blast group should be considered most at risk for
353 vestibular-related complaints for many years post-injury.

354 It has been known for some time that co-morbid psychiatric symptoms of
355 depression and anxiety exacerbate postconcussive symptoms.^{9,40} The current data are the
356 first to endorse these deleterious effects in a UK military mTBI sample, and likely only
357 fail to do so for PTSD because most participants reported significant PTSD symptoms so
358 together produced too little variability for the correlation to reach statistical significance.
359 But while all previous studies have identified dizziness/imbalance as a common
360 postconcussive symptom, they have overlooked the fact that the vestibular impairment
361 may explain other aspects of post-concussion syndrome. Here we confirm that when these
362 co-morbidities are controlled, vestibular impairment is separately associated with a range
363 of mental competencies. A strong association was found between the severity of self-
364 reported vestibular impairment and neuro-behavioural symptoms, as measured by the NSI
365 which contains items that probe sensory perception, motor co-ordination, sleep/fatigue,
366 mood and executive function. Additional analyses showed that when psychiatric co-
367 morbidity was taken into account, this strong association also held for both headache, an
368 especially common symptom of mTBI, and general disability as measured by the WHO-
369 DAS 2.0 which encompasses activities of daily living and social interaction. Interestingly,
370 these direct effects of vestibular impairment on postconcussive symptoms and general
371 disability held when scores from only the vertigo subdomain of the VSSL were entered
372 into the mediation analysis. This result gives support to the idea that the primary vestibular
373 deficit (as opposed to vestibular-induced psychiatric deficits which can be difficult to
374 disentangle from psychiatric deficits of alternative origin) contributed to the direct effects.

375 In addition to uncovering a direct link between vestibular and postconcussive
376 symptoms, the mediation analysis also uncovered an indirect link which incorporated co-

377 morbid psychiatric disturbance. Previous study tells us that vestibular disorder can
378 promote psychiatric disturbance so it is perhaps unsurprising that this pathway was also
379 linked to outcome. However, the relationship between psychiatric and vestibular function
380 is partly reciprocal which makes it difficult to reach strong inferences about causality, a
381 problem deepened by the fact that many military veterans with mTBI present with
382 psychiatric complaints that are partly non-vestibular in origin. Some insight can be
383 gleaned from the significant direct effects of the VSSL autonomic-anxiety subdomain on
384 outcome which suggest that, at the very least, the vestibular disturbance was exacerbating
385 symptoms of a psycho-somatic and somato-psychic nature.

386 Reflecting more broadly on the clinical presentation of the present study sample,
387 the constellation of vestibular, cognitive and affective symptoms mirrors the general
388 neuropsychiatric profile of civilians with diagnosed vestibular impairment but without a
389 history of mTBI.^{16,17} It further demonstrates the pervasive influence of the vestibular
390 system on human cognition,¹⁷ affecting higher-level processes rather than only the low-
391 level autonomic motor control processes with which it has traditionally been associated.
392 From a therapeutic perspective, the implication is that veterans with mTBI might broadly
393 benefit from a programme of vestibular rehabilitation. In preliminary support of this idea,
394 Kleffelgaard et al.⁴¹ showed in a case series of 3 civilians with mTBI and
395 dizziness/imbalance that a programme of vestibular rehabilitation was associated with
396 reduced psychological distress and improved health-related quality of life. In veterans,
397 Carric et al.⁴² showed a reduction in PTSD, as measured by the CAPS, after 2 weeks of
398 vestibular-ocular co-ordination involving gaze stabilisation, visual pursuit and saccadic
399 eye movement. Carric et al.⁴² also noted that treating PTSD as a physical injury rather than
400 as a psychiatric disorder helped lessen the stigma that veterans often feel towards help-
401 seeking which in turn could encourage treatment uptake.

402 Several methodological aspects limit the conclusions that can be drawn from the
403 current study. First and foremost, the absence of routine prospective screening for mTBI and
404 vestibular disorder meant that our investigations were founded on self-report data rather than
405 clinical examination which may have led to an over-estimation of effect. This over-estimation
406 may have been exacerbated by the relative ease with which vestibular and other
407 postconcussive symptoms can be conflated by clinically-naïve participants. Also, the study
408 was cross-sectional rather than longitudinal, and all participants were help-seeking and
409 receiving psychiatric support so although high in clinical need were not representative of the
410 broader veteran population. To this end, it would be informative to address the current study
411 questions in a participant sample with more varied mental health needs. On a related note, the
412 high prevalence of depression in the sample may help explain the relatively high number of
413 MCI failures which is of potential concern here because symptom exaggeration in one
414 neurological modality predicts exaggeration in other modalities.^{43,44,45,46} Given that this study
415 is the first to assess symptom exaggeration in UK veterans, this result should perhaps be
416 treated cautiously, not least because the study design does not allow the underlying drivers of
417 malingering and psychological dissociation to be separated. But for the present purpose it is
418 important to point out that the statistical outcomes from the mediation analyses are the same
419 if only those participants who passed the memory complaints inventory are included.

420 In conclusion, we report preliminary evidence that the long-term mental health of
421 help-seeking military veterans with mTBI is directly associated with the presence of
422 vestibular dysfunction. This finding is important because although anecdotal reports of
423 dizziness are common, vestibular function is not routinely assessed and, as a consequence,
424 neuro-otological referrals are not often made. Yet the current data raise the possibility that
425 by treating the vestibular disorder it may also be possible to treat a range of

426 neurobehavioral symptoms that accompany mTBI and which have so far proven difficult

427 to manage.

428

429 **References**

- 430 1. Hawley CA, de Burgh HT, Russell RJ, Mead A. Traumatic brain injury recorded in
431 the UK joint theatre trauma registry among the UK armed forces. *J Head Trauma*
432 *Rehabil.* 2015;30(1):E47-56.
- 433 2. MacGregor AJ, Shaffer RA, Dougherty AL, et al. Prevalence and psychological
434 correlates of traumatic brain injury in operation Iraqi freedom. *J Head Trauma*
435 *Rehabil.* 2010;25(1):1-8.
- 436 3. Hoge CW, McGurk D, Thomas JL, Cox AL, Engel CC, Castro CA. Mild traumatic
437 brain injury in US soldiers returning from Iraq. *N Engl J Med.* 2008;358(5):453-463.
- 438 4. Terrio H, Brenner LA, Ivins BJ, et al. Traumatic brain injury screening: Preliminary
439 findings in a US army brigade combat team. *J Head Trauma Rehabil.* 2009;24(1):14-
440 23.
- 441 5. Jones N, Fear NT, Rona R, et al. Mild traumatic brain injury (mTBI) among UK
442 military personnel whilst deployed in Afghanistan in 2011. *Brain Inj.* 2014;28(7):896-
443 899.
- 444 6. Rona RJ, Jones M, Fear NT, et al. Mild traumatic brain injury in UK military
445 personnel returning from Afghanistan and Iraq: Cohort and cross-sectional analyses. *J*
446 *Head Trauma Rehabil.* 2012;27(1):33-44.
- 447 7. McGlinchey RE, Milberg WP, Fonda JR, Fortier CB. A methodology for assessing
448 deployment trauma and its consequences in OEF/OIF/OND veterans: The TRACTS
449 longitudinal prospective cohort study. *Int J Methods Psychiatr Res.* 2017;26(3).
- 450 8. Cassidy JD, Carroll L, Peloso P, et al. Incidence, risk factors and prevention of mild
451 traumatic brain injury: Results of the WHO collaborating centre task force on mild
452 traumatic brain injury. *J Rehabil Med.* 2004;36(0):28-60.

- 453 9. Lippa SM, Fonda JR, Fortier CB, et al. Deployment-related psychiatric and
454 behavioural conditions and their association with functional disability in
455 OEF/OIF/OND veterans. *J Trauma Stress*. 2015;28(1):25-33.
- 456 10. Fausti SA, Wilmington DJ, Gallun FJ, Myers PJ, Henry JA. Auditory and vestibular
457 dysfunction associated with blast-related traumatic brain injury. *J Rehabil Res Dev*
458 2009;46(6).
- 459 11. Furman JM, Whitney SL. Central causes of dizziness. *Phys Ther*. 2000;80(2):179-
460 187.
- 461 12. Alhilali LM, Yaeger K, Collins M, Fakhran S. Detection of central white matter
462 injury underlying vestibulopathy after mild traumatic brain injury. *Radiology*.
463 2014;272(1):224-232.
- 464 13. Hoffer ME, Balaban C, Gottshall K, Balough BJ, Maddox MR, Penta JR. Blast
465 exposure: Vestibular consequences and associated characteristics. *Otol Neurotol*.
466 2010;31(2):232-236.
- 467 14. Pan T, Liao K, Roenigk K, Daly JJ, Walker MF. Static and dynamic postural stability
468 in veterans with combat-related mild traumatic brain injury. *Gait Posture*.
469 2015;42(4):550-557.
- 470 15. Chamelian L, Feinstein A. Outcome after mild to moderate traumatic brain injury:
471 The role of dizziness. *Arch Phys Med Rehabil*. 2004;85(10):1662-1666.
- 472 16. Grimm R, Hemenway W, Lebray P, Black F. The perilymph fistula syndrome defined
473 in mild head trauma. *Acta Otolaryngol*. 1989;108(sup464):1-40.
- 474 17. Smith L, Wilkinson D, Bodani M, Bicknell R, Surenthiran S. Short-term memory
475 impairment in vestibular patients can arise independently of psychiatric impairment,
476 fatigue, and sleeplessness. *J Neuropsychol*. In press.

- 477 18. Bigelow RT, Semenov YR, du Lac S, Hoffman HJ, Agrawal Y. Vestibular vertigo
478 and comorbid cognitive and psychiatric impairment: The 2008 national health
479 interview survey. *J Neurol Neurosurg Psychiatry*. 2016;87(4):367-372.
- 480 19. Haber YO, Chandler HK, Serrador JM. Symptoms associated with vestibular
481 impairment in veterans with posttraumatic stress disorder. *PloS One*.
482 2016;11(12):e0168803.
- 483 20. Hebert JR, Forster JE, Stearns-Yoder KA, Penzenik ME, Brenner LA. Persistent
484 symptoms and objectively measured balance performance among OEF/OIF veterans
485 with remote mild traumatic brain injury. *J Head Trauma Rehabil*. In press.
- 486 21. Balaban CD, Jacob RG, Furman JM. Neurologic bases for comorbidity of balance
487 disorders, anxiety disorders and migraine: Neurotherapeutic implications. *Exp Rev*
488 *Neurother*. 2011;11(3):379-394.
- 489 22. Lew HL, Guillory SB. Auditory dysfunction in traumatic brain injury. *Journal of*
490 *rehabilitation research and development*. 2007;44(7):921.
- 491 23. Corrigan JD, Bogner J. Initial reliability and validity of the Ohio State University TBI
492 identification method. *J Head Trauma Rehabil*. 2007;22(6):318-329.
- 493 24. Fortier CB, Amick MM, Grande L, et al. The Boston assessment of traumatic brain
494 injury-lifetime (BAT-L) semi-structured interview: Evidence of research utility and
495 validity. *J Head Trauma Rehabil*. 2014;29(1):89-98.
- 496 25. Management of Concussion/mTBI Working Group. VA/DoD clinical practice
497 guideline for management of Concussion/Mild traumatic brain injury. *J Rehabil Res*
498 *Dev*. 2009;46(6):CP1-68.
- 499 26. Yardley L, Masson E, Verschuur C, Haacke N, Luxon L. Symptoms, anxiety and
500 handicap in dizzy patients: Development of the vertigo symptom scale. *J Psychosom*
501 *Res*. 1992;36(8):731-741.

- 502 27. Cicerone KD, Kalmar K. Persistent postconcussive syndrome: Structure of subjective
503 complaints after mild traumatic brain injury. *Arch Phys Med Rehabil.* 1994;75(6):723.
- 504 28. Kosinski M, Bayliss M, Bjorner J, et al. A six-item short-form survey for measuring
505 headache impact: The HIT-6™. *Quality of Life Research.* 2003;12(8):963-974.
- 506 29. Johns MW. A new method for measuring daytime sleepiness: The Epworth sleepiness
507 scale. *Sleep.* 1991;14(6):540-545.
- 508 30. Weathers F, Litz B, Keane T, Palmieri P, Marx B, Schnurr P. The PTSD checklist for
509 DSM-5 (PCL-5). Washington, DC: US Department of Veterans Affairs. *National*
510 *Center for PTSD.* 2013.
- 511 31. Kessler R, Mroczek D. An update on the development of mental health screening
512 scales for the US national health interview scales. *Ann Arbor (MI): The University of*
513 *Michigan Institute for Social Research/Survey Research Center.* 1994.
- 514 32. Üstün, Kostanjsek, Chatterji S, Rehm J. *Measuring health and disability: Manual*
515 *for WHO disability assessment schedule WHODAS 2.0.* World Health Organization;
516 2010.
- 517 33. Green P, Allen L. Memory complaints inventory. *Edmonton, Canada: Green's*
518 *Publishing.* 2004.
- 519 34. Armistead-Jehle P, Grills CE, Bieu RK, Kulas JF. Clinical utility of the memory
520 complaints inventory to detect invalid test performance. *Clin Neuropsychol.*
521 2016;30(4):610-628.
- 522 35. Hayes Andrew F. Beyond Baron and Kenny: Statistical mediation analysis in the new
523 millennium. *Communication Monographs,* 76(4), 408-420.
- 524 36. Andrews G, Kemp A, Sunderland M, Von Korff M, Ustun TB. Normative data for the
525 12 item WHO disability assessment schedule 2.0. *PloS One.* 2009;4(12):e8343.

- 526 37. Department of Health. UK Chief Medical Officer's Alcohol Guidelines Review:
527 Summary of the Proposed New Guidelines. 2016.
- 528 38. Hayes AF. Model templates for PROCESS for SPSS and SAS. 2017;12:2013.
- 529 39. Robinson ME, Lindemer ER, Fonda JR, Milberg WP, McGlinchey RE, Salat DH.
530 Close-range blast exposure is associated with altered functional connectivity in
531 veterans independent of concussion symptoms at time of exposure. *Hum Brain Mapp.*
532 2015;36(3):911-922.
- 533 40. Porter KE, Stein MB, Martis B, et al. Postconcussive symptoms (PCS) following
534 combat-related traumatic brain injury (TBI) in veterans with posttraumatic stress
535 disorder (PTSD): Influence of TBI, PTSD, and depression on symptoms measured by
536 the neurobehavioral symptom inventory (NSI). *J Psychiatr Res.* 2018;102:8-13.
- 537 41. Kleffelgaard I, Soberg HL, Bruusgaard KA, Tamber AL, Langhammer B. Vestibular
538 rehabilitation after traumatic brain injury: Case series. *Phys Ther.* 2016;96(6):839-
539 849.
- 540 42. Carrick FR, McLellan K, Brock JB, Randall C, Oggero E. Evaluation of the
541 effectiveness of a novel brain and vestibular rehabilitation treatment modality in
542 PTSD patients who have suffered combat-related traumatic brain injuries. *Front*
543 *Public Health.* 2015;3:15.
- 544 43. Gervais RO, Ben-Porath YS, Wygant DB, Green P. Differential sensitivity of the
545 response bias scale (RBS) and MMPI-2 validity scales to memory complaints. *Clin*
546 *Neuropsychol.* 2008;22(6):1061-1079.
- 547 44. Green P, Rohling ML, Lees-Haley PR, III LMA. Effort has a greater effect on test
548 scores than severe brain injury in compensation claimants. *Brain injury.*
549 2001;15(12):1045-1060.

- 550 45. Armistead-Jehle P, Gervais RO, Green P. Memory complaints inventory and
551 symptom validity test performance in a clinical sample. *Arch Clin Neuropsychol*.
552 2012;27(7):725-734.
- 553 46. Armistead-Jehle P, Lange BJ, Green P. Comparison of neuropsychological and
554 balance performance validity testing. *Appl Neuropsychol Adult*. 2017;24(2):190-197.

Table 1. Sample Demographic ($n = 162$). Parenthesised values show standard deviation. $M =$ mean.

	n		n or $M (SD)$
Males	151	Part-time student	2
Females	11	Unemployed	53
Relationship Status		Retired	32
Married	92	Military Service Branch	
Divorced	39	Royal Navy	23
Single	29	Army	123
Widowed	2	Royal Airforce	11
Vocational Status		Royal Marines	6
Full-time employment	55	Armed Service History	
Part-time employment	19	Mean length of Service (years)	12.8 (7.2)
Full-time student	1	Mean deployments to a war zone	3.7 (1.8)

Table 2. Lifetime History and Prevalence of mTBI (n=117)

	<i>n</i>		<i>n</i>
Lifetime history ≥ 1 mTBI	117	Blunt & Blast	41
		Blast only	17
Hospitalised due to mTBI	82	Blunt only	59
mTBI with LOC	69	Blast Proximity	
		0-10 meters	38
Sustained >1 TBI	112	11-25 meters	15
Periods of repeated mTBI	57	26-100 meters	5
		Method of blunt injury	
History of moderate TBI	23	Road traffic	57
History of severe TBI	12	Sports-related	73
No TBI	10	Assault	54

Table 3. Frequency of comorbid symptoms in mTBI sample

Comorbid Symptoms	<i>n</i>	%	missing cases
PCS (NSI)	89	77.4	2
Vestibular (VSSL)	78	69.0	4
PTSD (PCL-5)	100	88.5	4
Depression/anxiety (K10)	104	92.9	5
Daytime sleepiness (ESS)	59	52.7	5
Headaches (HIT-6)	79	70.5	5

Table 4. Correlation matrices underpinning the exploratory NSI mediation analysis in which (a) responses to the 3 dizziness questions were omitted and (b) responses to only the vertigo-balance or autonomic-anxiety subdomains were included

(a)

	Total Effects	Direct Effects	Mediator	Indirect Effects	LCI	UCI
VSSL total score	$B = .50$ $p = < .001$	$B = .311$ $p = < .001$	PCL-5 Kessler	$B = .055$ $B = .134$	-.016 .055	.130 .245

(b)

	Total Effects	Direct Effects	Mediator	Indirect Effects	LCI	UCI
VSSL vertigo-balance	$B = .773$ $p = < .001$	$B = .540$ $p = < .001$	PCL-5 Kessler	$B = .092$ $B = .139$.017 .015	.222 .343
VSSL autonomic-anxiety	$B = 1.129$ $p = < .001$	$B = .767$ $p = < .001$	PCL-5 Kessler	$B = .100$ $B = .268$	-.109 .038	.287 .496

Table 5 (supplemental). Correlation matrix for the multiple linear regression analysis in which the NSI was the outcome variable ($N=113$)

	NSI		VSSL		PCL-5		K10	
NSI			$r = .69$	$p = <.001$	$r = .65$	$p = <.001$	$r = .66$	$p = <.001$
VSSL	$r = .69$	$p = <.001$			$r = .54$	$p = <.001$	$r = .44$	$p = <.001$
PCL-5	$r = .65$	$p = <.001$	$r = .54$	$p = <.001$			$r = .79$	$p = <.001$
K10	$r = .66$	$p = <.001$	$r = .44$	$p = <.001$	$r = .79$	$p = <.001$		

Table 6 (supplemental). Correlation matrix for the multiple linear regression analysis in which the HIT6 was the outcome variable ($N=112$)

	HIT6		VSSL		PCL-5		K10	
HIT6			$r = .51$	$p < .001$	$r = .49$	$p < .001$	$r = .54$	$p < .001$
VSSL	$r = .51$	$p < .001$			$r = .55$	$p < .001$	$r = .45$	$p < .001$
PCL-5	$r = .49$	$p < .001$	$r = .55$	$p < .001$			$r = .78$	$p < .001$
K10	$r = .54$	$p < .001$	$r = .45$	$p < .001$	$r = .78$	$p < .001$		

Table 7 (supplemental). Correlation matrix for the multiple linear regression analysis in which the WHODAS 2.0 was the outcome variable ($N=111$)

	WHODAS		VSSL		PCL-5		K10	
WHODAS			$r = .60$	$p < .001$	$r = .63$	$p < .001$	$r = .68$	$p < .001$
VSSL	$r = .60$	$p < .001$			$r = .55$	$p < .001$	$r = .45$	$p < .001$
PCL-5	$r = .63$	$p < .001$	$r = .55$	$p < .001$			$r = .78$	$p < .001$
K10	$r = .68$	$p < .001$	$r = .45$	$p < .001$	$r = .78$	$p < .001$		

Figure 1A Mediation analysis NSI ($N=113$)

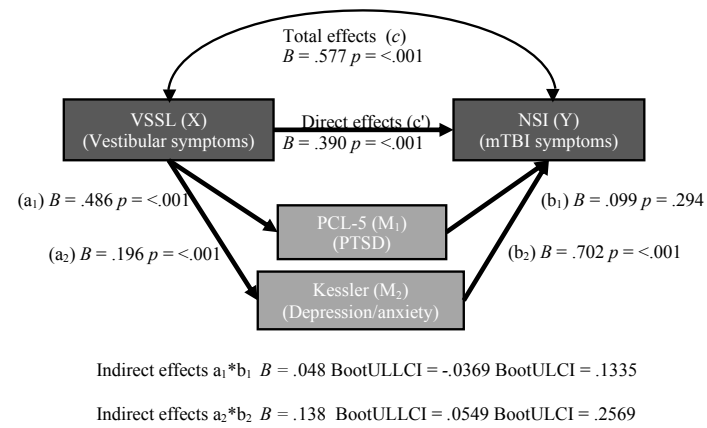


Figure 1B Mediation analysis HIT6 ($N = 112$)

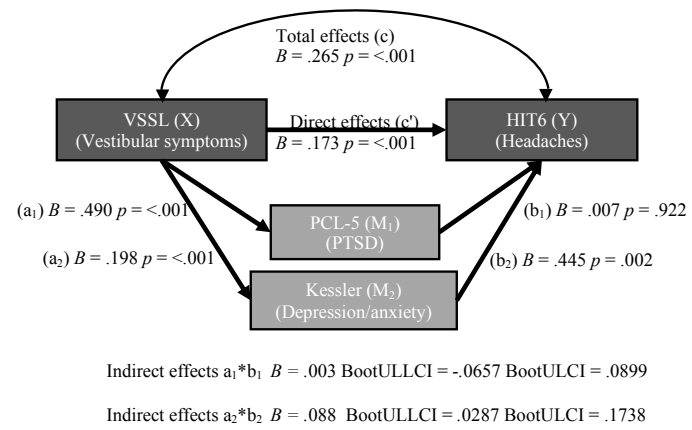


Figure 1C Mediation analysis WHODAS ($N = 111$)

