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Assessment of Potential Risk Factors for Development of Persistent Postural-Perceptual Dizziness: a case-control pilot study.

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Author contribution statement

Aaron Trinidad was responsible the principal investigator and responsible for the study design, conducting the study, data collection and preparation of the manuscript.

Paula Harman was responsible for liaison with study participants, liaising with research and development and ethics departments, conducting the study, supervision of study flow, with data processing and analysis and manuscript editing and proofreading.

Jon Stone was responsible for study design, supervision of the study and manuscript editing and proofreading.

Jeffrey P Staab was responsible for study design, supervision of the study and manuscript editing and proofreading.

Joel A Goebel was responsible for study design, supervision of the study and manuscript editing and proofreading.

Keywords

state anxiety, neuroticism, body vigilance, illness perceptions, PPPD

Abstract

Word count: 246

OBJECTIVES: (1) To assess whether neuroticism, state anxiety, and body vigilance are higher in patients with persistent postural-perceptual dizziness (PPPD) compared to a recovered vestibular patient group and a non-dizzy patient group; (2) To gather pilot data on illness perceptions of patients with PPPD. MATERIALS AND METHODS: 15 cases with PPPD and two control groups: (1) recovered vestibular patients (n=12) and (2) non-dizzy patients (no previous vestibular insult, n=12). Main outcome measures: Scores from the Big Five Inventory (BFI) of personality traits, Generalised Anxiety Disorder - 7 (GAD-7) scale, Body Vigilance Scale (BVS), Dizziness Handicap Inventory (DHI), modified Vertigo Symptom Scale (VSS) and Brief Illness Perception Questionnaire (BIPO). RESULTS: Compared to non-dizzy patients, PPPD cases had higher neuroticism ($p=0.02$), higher introversion ($p=0.008$), lower conscientiousness ($p=0.03$) and higher anxiety ($p=0.02$). There were no differences between PPPD cases and recovered vestibular patients in BFI and GAD-7. PPPD cases had higher body vigilance to dizziness than both control groups and their illness perceptions indicated higher levels of threat than recovered vestibular patients. CONCLUSION: PPPD patients showed statistically significant differences to non-dizzy patients, but not recovered vestibular controls in areas such as neuroticism and anxiety. Body vigilance was increased in PPPD patients when compared with both recovered vestibular and non-dizzy patient groups. PPPD patients also exhibited elements of negative illness perception suggesting that this may be the key element driving the development of PPPD. Large scale studies focusing on this area in the early stages following vestibular insult are needed.

Contribution to the field

The risk factors that make people prone to persistent postural-perceptual are still largely unknown but have been hypothesised to be underlying factors such as neuroticism, anxiety and increased body vigilance. This manuscript examines these factors in detail and suggests that the most important risk factors are increased body vigilance and illness perception.

Ethics statements

Studies involving animal subjects

Generated Statement: No animal studies are presented in this manuscript.

Studies involving human subjects

Generated Statement: The studies involving human participants were reviewed and approved by South West - Cornwall & Plymouth Research Ethics Committee. The patients/participants provided their written informed consent to participate in this study.

Inclusion of identifiable human data

Generated Statement: No potentially identifiable human images or data is presented in this study.

Data availability statement

Generated Statement: The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

In review

1 **Assessment of Potential Risk Factors for Development of Persistent Postural-Perceptual**
2 **Dizziness: a case-control pilot study.**

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17
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19
20 **Key words:** state anxiety; neuroticism; body vigilance; illness perceptions; PPPD.

21
22 **Abstract**

23
24 OBJECTIVES: (1) To assess whether neuroticism, state anxiety, and body vigilance are higher in
25 patients with persistent postural-perceptual dizziness (PPPD) compared to a recovered vestibular
26 patient group and a non-dizzy patient group; (2) To gather pilot data on illness perceptions of patients
27 with PPPD. MATERIALS AND METHODS: 15 cases with PPPD and two control groups: (1) recovered
28 vestibular patients (n=12) and (2) non-dizzy patients (no previous vestibular insult, n=12). Main outcome
29 measures: Scores from the Big Five Inventory (BFI) of personality traits, Generalised Anxiety Disorder
30 – 7 (GAD-7) scale, Body Vigilance Scale (BVS), Dizziness Handicap Inventory (DHI), modified Vertigo
31 Symptom Scale (VSS) and Brief Illness Perception Questionnaire (BIPQ). RESULTS: Compared to
32 non-dizzy patients, PPPD cases had higher neuroticism (p=0.02), higher introversion (p=0.008), lower
33 conscientiousness (p=0.03) and higher anxiety (p=0.02). There were no differences between PPPD
34 cases and recovered vestibular patients in BFI and GAD-7. PPPD cases had higher body vigilance to
35 dizziness than both control groups and their illness perceptions indicated higher levels of threat than
36 recovered vestibular patients. CONCLUSION: PPPD patients showed statistically significant
37 differences to non-dizzy patients, but not recovered vestibular controls in areas such as neuroticism
38 and anxiety. Body vigilance was increased in PPPD patients when compared with both recovered
39 vestibular and non-dizzy patient groups. PPPD patients also exhibited elements of negative illness
40 perception suggesting that this may be the key element driving the development of PPPD. Large scale
41 studies focusing on this area in the early stages following vestibular insult are needed.

42
43 **Introduction**

44 The diagnosis *persistent postural-perceptual dizziness (PPPD)* entered the 11th edition of the World
45 Health Organization's International Classification of Diseases (ICD-11 beta draft) in 2015 following a
46 consensus document on its diagnostic criteria created by Bárány Society for the International
47 Classification of Vestibular Disorders (ICVD) and the criteria for its diagnosis are outlined in Table 1¹⁻³.

48
49 PPPD is a relatively new diagnosis and to date it is still not clear what predisposes some people to it
50 following known triggers such as acute, episodic, or chronic vestibular syndromes, other neurological
51 or medical illnesses, or psychological distress. Several authors have shown that acute anxiety and body
52 vigilance predicted chronic dizziness after acute vestibulopathies⁴⁻⁸. A prospective study found that
53 psychological distress predicted severity of dizziness-related handicap among patients with various
54 vestibular disorders in the 12 months following tertiary consultation.⁹ Neuroticism, the personality trait
55 tendency to experience negative emotions or psychological distress in response to life events, has also
56 been identified as a possible predisposing risk factor in both PPPD and chronic subjective dizziness
57 (CSD), one of PPPD's precursors¹⁰⁻¹². In addition patients' appraisals and perceptions of their illness
58 have been shown to influence outcomes in a range of other medical conditions including vestibular

59 disorders^{13,14}. (Figure 1). Apart one study of neuroticism, however,¹⁰ these investigations were
60 conducted prior to publication of the ICD-11 and ICVD definitions of PPPD or included patients with
61 combinations of structural, metabolic, psychiatric, and functional causes of vestibular symptoms. As
62 such, they offer data to formulate hypotheses about roles that psychological variables and illness
63 perceptions may play in the development of PPPD. Confirmation or refutation of those hypotheses
64 requires investigations that include patients explicitly diagnosed with PPPD and carefully selected
65 comparison groups. In addition, it is yet to be determined if any of these factors are associated strongly
66 and uniquely enough with the onset of PPPD to be useful for early detection of the disorder.

67
68 As a first step in validating hypotheses about the relationship of psychological variables specifically to
69 PPPD and with the intent of designing a prospective trial to predict patients at risk for developing this
70 disorder, the primary aim of this current study was to gather pilot data to test the hypothesis that the
71 frequency of anxiety-related variables is higher in patients who meet ICVD criteria for PPPD compared
72 to those who suffered acute vestibulopathies but did not develop PPPD and patients without a history
73 of dizziness who were receiving treatment for other medical conditions. The second aim was to gather
74 pilot data on illness perceptions in patients with PPPD. Findings of an increased prevalence or severity
75 of anxiety-related variables or adverse illness perceptions would provide an impetus for conducting
76 fully-powered, prospective studies with the aim of identifying a risk profile for PPPD that could guide
77 early interventions for patients susceptible to developing this burdensome chronic dizziness condition.
78

79 **Methodology**

80 The study was conducted as a case-control observational study (www.clinicaltrials.gov, reference
81 NCT03930485, with ethical approval from South West – Cornwall & Plymouth Research Ethics
82 Committee). All participants (both cases and controls) were aged ≥ 18 years old and were able to provide
83 informed consent. Any participants who were < 18 years old and unable to provide informed consent
84 were excluded from the study.
85

86 Data collected

87 All participants (cases, recovered group and healthy group) provided written informed consent before
88 then being asked to complete the Big Five Inventory (BFI) of personality traits, the Generalised Anxiety
89 Disorders Scale – 7 (GAD-7), the Body Vigilance Scale (BVS), the Dizziness Handicap Inventory (DHI),
90 the short form of the Vertigo Symptom Scale (VSS), and the Brief Illness Perception Questionnaire
91 (BIPQ). The BFI consists of 44 questions that assess the five core human personality traits of
92 neuroticism (tendency toward pessimistic worry), extraversion (outgoing nature), openness (to new
93 ideas and experiences), agreeableness (affability and warmth), and conscientiousness (diligence and
94 dutifulness) and provides standardized scores against population norms. Testers respond to the
95 questions with degrees of agreement or disagreement on a 5-point Likert scale. For each personality
96 trait, a mean score of higher than 2.5 suggests a tendency towards that trait. The GAD-7 consists of
97 seven questions that measure the severity of state anxiety. The BVS consists of four questions: the first
98 three measure sensitivity and attentiveness to bodily sensations in general; the fourth question
99 measures attentiveness to 15 specific somatic symptoms, including five that are germane to patients
100 with vestibular disorders (dizziness, nausea, faintness, feelings of unreality, and feelings detached from
101 one's self). Testers respond to the questions on an 11 point Likert-like scale ranging from 0 (Not at all
102 like me) to 10 (Extremely like me). A mean score on higher than 5.0 suggests a tendency towards
103 strong agreement with the question. The BVS total score is the sum of the answers to questions one to
104 four. The DHI contains 25 questions that measure the severity of handicap due to dizziness-related
105 physical and emotional symptoms and interference with functioning. The short form VSS includes 15
106 questions, eight that measure severity of vertiginous symptoms and seven that measure severity of
107 associated autonomic/anxiety symptoms. The BIPQ consists of 9 questions that assess respondents'
108 understanding, emotional response, and sense of control of their illness, as well as concerns about its
109 causes, consequences, clinical course, and likelihood of treatment response. The DHI, VSS and BIPQ
110 were administered to the PPPD group only as they were the only ones with active dizziness symptoms
111 required to make sense of the questionnaires.
112

113 Statistical analysis (performed using SPSS Statistics v26)

114 Statistical analyses were confined to valid outputs from the questionnaires that tested our hypotheses.
115 As the DHI, VSS, and GAD-7 have not been validated for item-by-item analyses and the BIPQ has no
116 total score, analyses were limited to: BFI – scores for the 5 factors; GAD-7 – total score only; BVS –

117 individual item scores; DHI – total score only; VSS – total and two subscale scores; BIPQ – individual
118 items only.

119

120 *BFI, GAD-7 & BVS*

121 Each variable was checked for normality (skewness, kurtosis, Shapiro-Wilk's test), however very few
122 of the variables were normally distributed. Due to this, and the low sample size, non-parametric tests
123 were used. Due to having three independent variables (cases, recovered group, healthy group), an
124 Independent-Samples Kruskal-Wallis test was performed. If a statistically significant result was found,
125 then a *post hoc* pairwise comparison was conducted to determine which of the study groups were
126 statistically different from each other. Statistical significance was determined at $p < 0.05$. Significance
127 values for pairwise comparisons significance values were adjusted using Bonferroni correction for
128 multiple tests and were reported as their adjusted values. Effect sizes, η^2 , were calculated from the
129 Kruskal-Wallis H-value and were interpreted per usual convention as $\eta^2 < 0.06$ (small), $0.06 \leq \eta^2 < 0.14$
130 (medium), and $\eta^2 \geq 0.14$ (large).

131

132 **Results**

133 Recruitment

134 *Cases*

135 The clinical care team at the Department of Otolaryngology, Southend University Hospital NHS
136 Foundation Trust reviewed medical records of current and past patients who were evaluated between
137 January 2019 and January 2020. Eighteen patients who had been given a diagnosis of PPPD in
138 accordance with ICVD criteria (Table 1) during that time period were consecutively asked to take part
139 in the study. All 18 agreed to participate but only 15 completed and returned the questionnaire (see
140 below). These 15 patients were included in the PPPD group with the 3 non-responders being excluded
141 from the study.

142

143 *Controls*

144 Two sex- and age-matched (± 5 years) comparison groups were identified. The first group consisted
145 of patients who had sustained a peripheral vestibular insult but did not develop PPPD (recovered
146 vestibular patient controls). Participants in this group were all consecutively recruited from the dizziness
147 and balance clinic, deemed to have recovered from their vestibular insult and not progressed to PPPD.
148 To be included as a recovered vestibular patient control, patients had to confirm that they had not
149 experienced any vertigo or dizziness within the last year and were currently asymptomatic. As
150 labyrinthine function and symptoms in recovered vestibular patients correlate poorly^{15,16}, it was not
151 deemed necessary to subject controls within this group to further vestibular function testing.
152 Confirmation of an asymptomatic state was taken as evidence of full compensation from previous
153 vestibular insult.

154

155 The second group consisted of patients from both the general ENT clinic and other non-ENT clinics
156 who had never sustained a vestibular insult (non-dizzy patient controls). This group included any patient
157 who was being followed up for a non-vestibular condition. Patients were asked whether they had ever
158 experienced vertigo and dysequilibrium in the past or whether they had ever been diagnosed with a
159 condition that could cause vertigo and only those who had not were asked to participate. The conditions
160 that these patients were being followed up for included rhinitis (n=2), otitis externa (n=1), tinnitus (n=1),
161 epistaxis (n=1), tympanic membrane perforation (n=1), single-sided deafness (n=1), chronic back pain
162 (n=1), knee osteoarthritis (n=1), deep vein thrombosis (n=1), anal polyps (n=1) and COPD (n=1). The
163 purpose of the non-dizzy comparison group was to control for the state of being ill versus being
164 healthy. The psychological measures that were investigated are potentially affected by overall health
165 status but vary little with respect to specific types of medical illness.

166

167 Demographics

168 15 PPPD cases (13 (86.7%) females and 2 males, with a mean age was 63.7 years) were matched
169 with 12 recovered vestibular controls (10 females (83.3%), mean age 63.8 years) and 12 non-dizzy
170 controls (10 females (83.3%), mean age 62.6 years). The mean duration from diagnosis of PPPD was
171 5.7 months (range: 0 – 13 months) and the mean duration of PPPD symptoms was 79.5 months (range:
172 8 – 300 months). In the PPPD group vestibular neuronitis (VN) and benign paroxysmal positional vertigo
173 (BPPV) were the two most common triggers (both: n=4, 26.7%), followed by Ménière's disease (n=3,
174 20%), psychological distress (n=3, 20%) and gentamicin-induced vestibular failure (n=1, 6.7%). Of the
175 three patients who developed PPPD following psychological distress, all three cited bereavement of a

176 spouse (n=2) or parent (n=1) as the trigger of their symptoms. One third of the group were on psychiatric
177 medication. (See Table 2) The vestibular insults in the recovered vestibular group were BPPV (n=6,
178 50%), VN (n=4, 33.3%), Ménière's disease (treated with intratympanic gentamicin therapy; n=1) and
179 vestibular schwannoma (managed with stereotactic radiotherapy; n=1).

180 181 Big Five Inventory

182 There was a statistically significant difference between the three study groups in neuroticism ($p=0.01$;
183 $\eta^2=0.16$, large effect), extroversion ($p=0.01$, $\eta^2=0.20$, large effect), and conscientiousness ($p=0.03$;
184 $\eta^2=0.14$, large effect), but not openness ($p=0.4$). or Agreeableness trended toward a significant
185 difference ($p=0.09$) with a low medium effect; $\eta^2=0.08$. Pairwise comparison revealed that these results
186 were largely due to differences between patients with PPPD and non-dizzy controls. Patients with
187 PPPD had higher neuroticism than non-dizzy controls ($p=0.02$; $\eta^2=0.43$, large effect) whilst non-dizzy
188 controls were more extroverted ($p=0.008$; $\eta^2=0.49$, large effect) and more conscientious ($p=0.03$;
189 $\eta^2=0.41$, large effect) than patients with PPPD. A pairwise comparison between patients with PPPD
190 and recovered vestibular controls for neuroticism approached significance ($p=0.05$). The effect size,
191 $\eta^2=0.38$, was large indicating a clinically meaningful difference that a larger sample would have revealed
192 as statistically significant). (See Table 3).

193 194 Generalised Anxiety & Depression – 7

195 With respect to the overall GAD-7 score, there was a statistically significant difference among groups
196 ($p<0.02$; $\eta^2=0.18$, large effect). The mean score for PPPD cases was 10.6; for recovered vestibular
197 controls was 4.6; for non-dizzy controls was 4.1. Pairwise analysis showed that PPPD cases were
198 statistically significantly more anxious than non-dizzy controls ($p=0.02$; $\eta^2=0.43$, large effect) and
199 trended toward a difference from recovered vestibular controls ($p=0.07$); Again, a large effect size,
200 $\eta^2=0.49$, suggested a clinically meaningful difference that missed statistical significance due to the
201 sample size.

202 203 Body Vigilance Scale

204 There was a statistically significant difference among the study groups in the scores of two subsets of
205 question 4 of the BVS pertaining to how much attention was paid to specific body sensations: feelings
206 of dizziness ($p<0.0001$; $\eta^2=0.58$, large effect) and unreality ($p=0.02$; $\eta^2=0.15$, large effect). In pairwise
207 comparisons, PPPD cases were found to pay more attention to feelings of dizziness than both control
208 group (versus recovered vestibular controls: $p=0.002$, $\eta^2=0.53$, large effect; versus non-dizzy controls:
209 $p<0.0001$, $\eta^2=0.72$, large effect) and to feelings of unreality than non-dizzy controls: $p=0.02$, $\eta^2=0.36$,
210 large effect). (See Table 4).

211 212 Brief Illness Perception Questionnaire

213 Patients with PPPD agreed quite strongly that PPPD affected their life severely and generally felt that
214 it would last a long time. There was a slightly weaker tendency for patients to indicate feeling like they
215 had no control over their illness and that the treatment they were on for PPPD was unlikely to help their
216 symptoms. There were stronger tendencies for patients with PPPD to consider that their symptoms
217 were severe, concerning, and affecting them emotionally. However they tended to agree that they
218 understood their illness. When asked to rank the three most likely factors causing their problem, only
219 one third of the patients listed psychological problems, although the wording could have been
220 interpreted as the initial trigger rather than the current mechanism of the symptoms. (Table 5).

221 222 DHI & VSS

223 The mean total DHI score was 29.3/100 (range: 11 – 43, s.d.=9.8), which is at the upper border of the
224 mild range (0 – 30) on this questionnaire (Whitney, *et al.* (2004))¹⁷. The mean total VSS score was 28.7
225 (range: 10 – 49; s.d.=10.8).

226 227 Post-hoc analysis

228 A post-hoc analysis was performed on the data set for BFI, GAD-7 and BVS after removing cases who
229 developed PPPD following psychological trauma (n=3), leaving a more homogeneous subgroup of 12
230 patients who developed PPPD following peripheral vestibular illnesses, in total (11 females, 1 male;
231 mean age 62.8 years; mean months from diagnosis, 6; mean duration of symptoms, 86 months). All
232 controls (12 recovered vestibular controls and 12 non-dizzy controls) were kept in the data set. The
233 focus of this sub-analysis was therefore on structural vestibular triggers of PPPD likely to present to the
234 ENT surgeon. The statistical treatment of this data set was identical to that of the original data set. The

235 post-hoc analysis showed a statistically significant result in one question of the BVS only: PPPD patients
236 were found to pay more attention to feelings of dizziness than both controls (versus recovered vestibular
237 controls: $p=0.007$; versus non-dizzy controls: $p<0.0001$) than both control groups. There were no
238 statistically significant differences between patients who developed PPPD after a vestibular illness and
239 either control group with respect to the BFI or GAD-7 questionnaires.

240 241 **Discussion**

242 The processes thought to give rise to and then drive PPPD are a combination of those described for its
243 precursors, namely phobic postural vertigo, space-motion discomfort, visual vertigo and chronic
244 subjective dizziness². Anxiety and anxiety-related personality traits, in particular neuroticism, have been
245 described as possible predisposing factors, making the affected individual prone to a hypervigilant state
246 of increased introspective self-monitoring that arises from fear of further attacks of vertigo or the
247 consequences of being dizzy during or following the episode of acute vestibular disease^{7,10,11,18-25}. Yagi,
248 *et al.* (2019) have recently developed a PPPD severity questionnaire (the Niigata PPPD Questionnaire)
249 that reflects the diagnostic criteria of PPPD²⁶. Even more recently, Powell, *et al.* (2020) describe PPPD
250 as a complex neurological condition that includes broad perceptual factors and suggest that some
251 individuals' brains are predisposed to generalised cross-modal sensory-overload, giving rise to
252 vulnerability to severe PPPD should a vestibular insult occur²⁷. What remains to be determined is
253 whether pre-existing psychological risk factors that can help in predicting who might be at risk of
254 developing PPPD after an acute vestibular injury, thus allowing for the institution of early treatment³.

255
256 Neuroticism is thought to be one of the key risk factors for the development of PPPD and refers to
257 relatively stable tendencies to respond with negative emotions to threat, frustration or loss²⁸. Individuals
258 who score highly on the BFI for neuroticism are more prone to anxiety amongst other negative emotions.
259 In a functional MRI (fMRI) study by Indovina, *et al.* (2015) it was shown that reduced activation in human
260 analogue of the parieto-insular vestibular cortex (PIVC), hippocampus, anterior insula, inferior frontal
261 gyrus and anterior cingulate cortex, as well as connectivity changes among these regions, may be
262 linked to long-term vestibular symptoms in patients with CSD²⁹. Also in a fMRI study, Ricelli, *et al.* (2017)
263 showed that individual differences in neuroticism were significantly associated with changes in the
264 activity and functional connectivity patterns within visuo-vestibular and anxiety-related systems during
265 simulated vertical self-motion³⁰. Similarly, Passamonti, *et al.* (2018) have shown neuroticism to increase
266 the activity and connectivity of neural networks that mediate attention to visual motion cues during
267 vertical motion. They suggest that this mechanism may mediate visual control of balance in neurotic
268 patients with PPPD³¹. In our study, PPPD patients were found to be more neurotic than healthy controls.
269 When compared with recovered controls, the result approached significance only, though the effect size
270 calculation indicated that this negative finding may have been a Type II error given our small sample
271 size. Our study also showed PPPD patients to be more introverted and less conscientious than non-
272 dizzy controls, in keeping with previous research findings by Staab, *et al.* (2014) with respect to chronic
273 subjective dizziness¹⁰.

274
275 Anxiety is a crucial factor in persisting dizziness⁴. The prevalence of anxiety in PPPD has been the
276 focus of one of the treatment modalities, namely cognitive behavioural therapy (CBT)³². Toshishige, *et al.*
277 (2020) have recently demonstrated in a study of 34 patients with PPPD that the presence of comorbid
278 anxiety disorders predicted a considerable improvement of DHI score from pre-treatment to 6-month
279 following CBT³³. Our data showed a significant difference in anxiety levels between PPPD cases and
280 non-dizzy controls. The comparison with recovered vestibular controls did not reach statistical
281 significance, but again the effect size pointed to a Type II error.

282 .
283
284 It is interesting that the primary comparisons of all PPPD cases to recovered vestibular controls and
285 the post-hoc analysis limited to cases of PPPD following vestibular illnesses found no significantly
286 greater neuroticism or anxiety in those with PPPD. It may be that in a larger cohort, both factors would
287 be significantly higher in PPPD.

288
289 Alongside anxiety, a high BVS in the setting of acute vestibular disorders has been shown to predict
290 persistent PPPD-like dizziness far better than measures of structural vestibular deficits^{4-7,32}. In a
291 prospective longitudinal study, Heinrichs, *et al.* (2007) assessed fear of bodily sensations and
292 cognitions related to anxiety at the time of hospital admission and three months later in 43 patients with
293 an episode of VN or BPPV. They showed that the interaction between fear of bodily sensations within

294 the first two weeks after admission and the type of vestibular disorder predicted the extent of dizzy
295 complaints three months later⁵. Our study reflects these findings, with attention to a feeling of dizziness
296 being found to be highly statistically significant in PPPD with respect to the BVS when compared with
297 both control groups. Our post-hoc analysis also supports this notion by demonstrating the importance
298 of heightened body vigilance even in a group of patients developing PPPD after vestibular insult.
299

300 There is evidence in other areas of medicine that supports the notion that negative illness perception is
301 independently linked to all-cause mortality and can strongly influence recovery from illness which can
302 be slower than in other patients³⁴⁻³⁶. Illness perception is seen as an important and potentially modifiable
303 risk factor to target in future disease interventions and intervention has already been shown to reduce
304 illness anxiety, which has relevance in this study^{35,37}. One interesting finding in our study that despite
305 PPPD patients being found to be more neurotic and anxious than healthy controls, only one third of
306 them felt that psychological factors were contributing to their symptoms. This shows similarities to other
307 functional disorders. In a controlled study of 107 patients with functional weakness, Stone, *et al.* (2010)
308 showed that these patients tend to reject psychological factors as potentially causal factors³⁸. They also
309 demonstrated similar findings, though to a lesser degree, in patients with non-epileptic seizures³⁹. In
310 PPPD, one potential for this finding may be due to the fact that whilst patients experience their dizziness
311 most of the time, they may not necessarily attribute their symptoms to anxiety-related factors or consider
312 anxiety to be a secondary consequence rather than a contributor to their symptoms. Stigmatisation of
313 mental health issues could also play a role, especially in male patients. Targeted patient education on
314 the central role anxiety plays in PPPD could help in addressing this misperception and improving illness
315 perception.
316

317 The results of this study support hypotheses derived from investigations of the predecessors of PPPD
318 that anxiety-related factors play important roles in promoting the development of the disorder following
319 conditions that cause vestibular symptoms or disturb balance function, including acute vestibular
320 disorders. However, these results offer a sharper focus, suggesting specifically that heightened body
321 vigilance about dizziness and adverse perceptions of illness may distinguish patients likely to develop
322 PPPD from those more likely to recover from acute illnesses without clinically significant sequelae. The
323 ultimate goal of this line of research is to develop a risk profile that can be used reliably to identify
324 patients susceptible to PPPD so that they may receive early and hopefully preventative interventions.
325 Such a profile is likely to consist of clinical variables present at the time of an acute vestibulopathy (e.g.,
326 anxiety-related personality traits, state anxiety) and ones that emerge in the immediate aftermath of
327 acute illness before the onset of chronic morbidity (e.g., adverse illness perceptions).
328

329 *Study limitations*

330 The participant numbers in this exploratory study were small, so no conclusions may be drawn from the
331 results. However, the investigation accomplished its stated objective by gathering pilot data from
332 patients explicitly diagnosed with PPPD to inform the design of more definitive investigations of risk
333 factors and potential early indicators of the disorder.
334

335 The study was retrospective and carried with it the inherent problems associated with retrospective
336 studies. Whilst a systematic data collection method was employed, it was collected from patients after
337 they had developed PPPD and at differing times from the onset, thus representing a heterogeneous
338 group.
339

340 In our main analysis, PPPD cases were included regardless of their initiating insult, vestibular or
341 otherwise, despite all members of the recovered group having a history of vestibular insult only. This is
342 because the ICVD criteria do not sub-categorise PPPD by type of precipitating event. Our post-hoc
343 analysis suggested that this may have had an effect on our results as the comparisons limited to
344 patients who developed PPPD following a vestibular disorder identified a narrower range of differences
345 than the full PPPD cohort compared to recovered controls. Potential differences risk factors for
346 development of PPPD following different precipitants merits future study.
347

348 Interestingly, our PPPD group was older and consisted of more women than most other reports of PPPD
349 and CSD. This may reflect differences in referrals patterns to various clinical centers around the world
350 and might make our data uncomparable with other studies.
351

352 **Conclusion**

353 The data gathered in this pilot study support the design and conduct of fully powered prospective
354 investigations of neuroticism, state anxiety, body vigilance and aberrant illness perceptions as risk
355 factors and contributors to the onset of PPPD that could be formulated into a risk profile to be used for
356 early detection of the disorder in clinical practice.

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452 **Figure 1.** Potential risk factors for PPPD include, from left to right, anxiety-related personality traits
453 (primarily neuroticism and introversion) that predate the onset of vestibular symptoms, high levels of
454 state anxiety and body vigilance that coincide with the onset of vestibular symptoms, and adverse illness
455 perceptions and dizziness-related handicap that emerge as the course of illness progresses toward
456 PPPD rather than recovery.
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Table 1. Criteria for the diagnosis of persistent postural-perceptual dizziness (PPPD) as outlined by the Committee for the Classification of Vestibular Disorders of the Bárány Society (CCBS)².

Criteria*	Description	Qualifiers
A	One or more symptoms of dizziness, unsteadiness, or non-spinning vertigo are present on most days for 3 months or more.	<ol style="list-style-type: none">1. Symptoms last for prolonged (hours long) periods of time but may wax and wane in severity.2. Symptoms need not be present continuously throughout the entire day.
B	Persistent symptoms occur without specific provocation, but are exacerbated by three factors:	<ol style="list-style-type: none">1. Upright posture,2. Active or passive motion without regard to direction or position, or3. Exposure to moving visual stimuli or complex visual patterns.
C	The disorder is precipitated by conditions that cause vertigo, unsteadiness, dizziness, or problems with balance including acute, episodic, or chronic vestibular syndromes, other neurological or medical illnesses, or psychological distress.	<ol style="list-style-type: none">1. When the precipitant is an acute or episodic condition, symptoms settle into the pattern of criterion A as the precipitant resolves, but they may occur intermittently at first, and then consolidate into a persistent course.2. When the precipitant is a chronic syndrome, symptoms may develop slowly at first and worsen gradually.
D	Symptoms cause significant distress or functional impairment.	
E	Symptoms are not better accounted for by another disease or disorder.	

475 *All five criteria A-E must be fulfilled to make the diagnosis of PPPD

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491 **Table 2.** Demographic data of cases with PPPD.

Cases	Age	Sex	Duration of PPPD symptoms(months)	Precipitating condition	Psychiatric medications
1	78	F	300	BPPV	None
2	34	F	10	Vestibular neuronitis	None
3	67	F	14	Vestibular neuronitis	Fluoxetine
4	69	M	21	Psychological distress	None
5	69	F	8	Psychological distress	Sertraline
6	82	F	14	BPPV	None
7	73	F	9	Gentamicin-induced vestibular failure	None
8	69	F	18	Ménière's disease	None
9	61	F	21	Vestibular neuronitis	None
10	59	F	300	Ménière's disease	Amitriptyline, duloxetine, quetiapine
11	63	F	132	Psychological distress	None
12	49	F	108	Ménière's disease	None
13	47	F	216	BPPV	Fluoxetine
14	70	M	14	BPPV	Sertraline
15	65	F	8	Vestibular neuronitis	None
Mean	62.6		79.5		

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Table 3. Big Five Inventory – Patients with PPPD patients and comparison groups.

Domain	Group	Mean	Std. Error	Mean Ranks	Kruskal-Wallis test Sig. (p)	Pairwise Sample	Sig. (p)	Adj. sig* (p)
Agreeableness	PPPD (15)	3.9	0.13	15.63	0.09	RC ^a -HC ^b	-	-
	RC (12)	4.1	0.15	20.2		RC-PPPD	-	-
	HC (12)	4.4	0.2	27.1		HC-PPPD	-	-
Extraversion	PPPD (15)	2.7	0.2	13.9	0.01	RC-HC	0.15	0.46
	RC (12)	3.4	0.2	20.5		RC-PPPD	0.13	0.4
	HC (12)	3.8	0.1	27.1		HC-PPPD	0.003	0.008
Conscientiousness	PPPD (15)	3.6	0.2	14.2	0.03	RC-HC	0.5	1.0
	RC (12)	4.1	0.1	22.0		RC-PPPD	0.08	0.23
	HC (12)	4.2	0.1	25.3		HC-PPPD	0.01	0.03
Openness	PPPD (15)	3.2	0.2	17.3	0.4	RC-HC	-	-
	RC (12)	3.4	0.2	19.9		RC-PPPD	-	-
	HC (12)	3.6	0.2	23.5		HC-PPPD	-	-
Neuroticism	PPPD (15)	3.5	0.2	26.8	0.01	RC-HC	0.8	1.0
	RC (12)	2.6	0.2	16.4		RC-PPPD	0.02	0.05
	HC (12)	2.5	0.2	15.1		HC-PPPD	0.008	0.02

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*significance values adjusted by Bonferroni correction for multiple tests

^aRC – Recovered Controls (recovered vestibular patients)

^bHC – Healthy Controls (non-dizzy patients)

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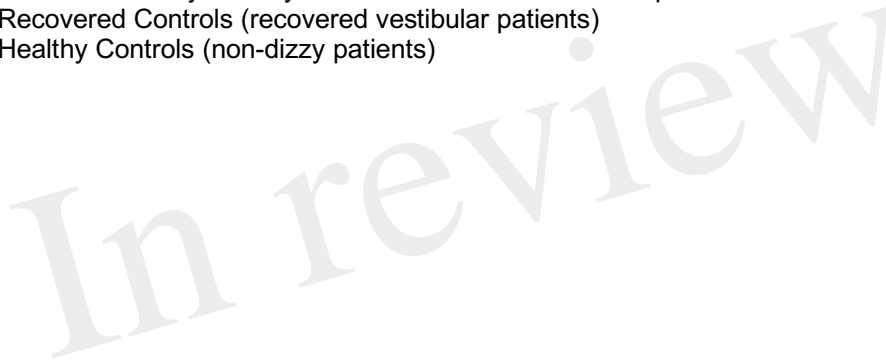


Table 4. Body Vigilance Scale (BVS) – Patients with PPPD patients and comparison groups.

	Group	Mean	Std. Error	Mean Ranks	Kruskal-Wallis test Sig. (p)	Pairwise Sample	Sig. (p)	Adj. sig* (p)
Q1. "I am the kind of person who pays close attention to internal body sensations."	PPPD (15)	6.1	0.5	25.9	0.04	RC-HC	0.92	1.0
	RC ^a (12)	3.5	0.9	16.1		RC-PPPD	0.03	0.08
	HC ^b (12)	3.6	1.0	16.5		HC-PPPD	0.03	0.1
Q2. "I am very sensitive to changes in my internal body sensations."	PPPD (15)	5.5	0.7	23.7	0.3	RC-HC	-	-
	RC (12)	3.5	0.9	17.0		RC-PPPD	-	-
	HC (12)	4.0	1.2	18.4		HC-PPPD	-	-
Q3. On average, how much time do you spend each day scanning your body for sensations?	PPPD (15)	29.3	7.3	25.5	0.03	RC-HC	0.9	1.0
	RC (12)	6.7	3.6	16.8		RC-PPPD	0.03	0.09
	HC (12)	9.2	6.1	16.3		HC-PPPD	0.02	0.07
Q4. Rate how much attention you pay to each of the following sensations using this scale:								
Q4.1. heart palpitations	PPPD (15)	3.3	1.0	21.7	0.6	RC-HC	-	-
	RC (12)	2.9	1.0	20.7		RC-PPPD	-	-
	HC (12)	2.2	0.9	17.3		HC-PPPD	-	-
Q4.2. chest pain/discomfort	PPPD (15)	3.5	1.0	23.4	0.2	RC-HC	-	-
	RC (12)	2.4	1.0	19.6		RC-PPPD	-	-
	HC (12)	1.3	0.7	16.2		HC-PPPD	-	-
Q4.3. numbness	PPPD (15)	3.5	1.0	22.9	0.3	RC-HC	-	-
	RC (12)	2.3	0.7	20.3		RC-PPPD	-	-
	HC (12)	1.4	0.8	16.1		HC-PPPD	-	-
Q4.4. tingling	PPPD (15)	3.5	1.0	23.9	0.2	RC-HC	-	-
	RC (12)	1.7	0.6	17.6		RC-PPPD	-	-
	HC (12)	1.7	0.8	17.5		HC-PPPD	-	-
Q4.5. shortness of breath/smothering	PPPD (15)	4.2	1.1	22.2	0.6	RC-HC	-	-
	RC (12)	2.8	1.0	18.3		RC-PPPD	-	-
	HC (12)	3.0	1.0	19.0		HC-PPPD	-	-
Q4.6. faintness	PPPD (15)	3.6	1.0	23.5	0.2	RC-HC	-	-
	RC (12)	2.0	0.7	19.7		RC-PPPD	-	-
	HC (12)	1.4	0.9	16.0		HC-PPPD	-	-
Q4.7. vision changes	PPPD (15)	4.7	0.8	23.5	0.3	RC-HC	-	-
	RC (12)	2.9	0.8	17.3		RC-PPPD	-	-
	HC (12)	3.2	1.1	18.3		HC-PPPD	-	-
Q4.8. feelings of unreality	PPPD (15)	3.1	0.9	25.1	0.02	RC-HC	0.4	1.0
	RC (12)	0.8	0.4	18.5		RC-PPPD	0.08	0.2
	HC (12)	0.8	0.8	15.1		HC-PPPD	0.008	0.02
Q4.9. feeling detached from self	PPPD (15)	3.2	0.9	24.6	0.1	RC-HC	-	-
	RC (12)	0.7	0.3	17.3		RC-PPPD	-	-
	HC (12)	1.7	1.0	17.0		HC-PPPD	-	-
Q4.10. dizziness	PPPD (15)	8.2	0.5	30.2	0.0	RC-HC	0.3	0.8
	RC (12)	2.2	0.9	16.0		RC-PPPD	0.001	0.002
	HC (12)	0.8	0.8	11.2		HC-PPPD	0.0	0.0
Q4.11. hot flash	PPPD (15)	3.7	1.0	22.9	0.2	RC-HC	-	-
	RC (12)	1.3	0.8	15.8		RC-PPPD	-	-
	HC (12)	3.1	1.0	20.6		HC-PPPD	-	-
Q4.12. sweating/clammy hands	PPPD (15)	2.7	0.9	21.7	0.7	RC-HC	-	-
	RC (12)	1.5	0.8	18.1		RC-PPPD	-	-
	HC (12)	2.3	0.9	19.8		HC-PPPD	-	-
Q4.13. upset stomach	PPPD (15)	4.1	0.9	23.7	0.2	RC-HC	-	-
	RC (12)	1.9	0.8	15.7		RC-PPPD	-	-
	HC (12)	3.2	1.0	19.6		HC-PPPD	-	-
Q4.14. nausea	PPPD (15)	3.5	0.8	24.1	0.1	RC-HC	-	-
	RC (12)	2.8	1.0	20.2		RC-PPPD	-	-
	HC (12)	1.1	0.7	14.6		HC-PPPD	-	-
Q4.13. choking/throat closing	PPPD (15)	4.0	1.0	24.8	0.1	RC-HC	-	-
	RC (12)	1.8	0.9	17.9		RC-PPPD	-	-
	HC (12)	1.3	0.8	16.1		HC-PPPD	-	-

556 *significance values adjusted by Bonferroni correction for multiple tests

557 ^aRC – Recovered Controls (recovered vestibular patients)

558 ^bHC – Healthy Controls (non-dizzy patients)

564 **Table 5.** Brief Illness Perception Questionnaire (BIPQ) – descriptive statistics for PPPD cases.

	N	Mean	Std. Deviation
Q1. How much does your illness affect your life? (0=no affect at all, 10= severely affects my life)	15	7.4	2.6
Q2. How long do you think your illness will continue? (0= a very short time,; 10= forever)	14	8.5	2.4
Q3. How much control do you feel you have over your illness? (0=absolutely no control, 10=extreme amount of control)	15	4.1	4.0
Q4. How much do you think your treatment can help your illness? (0=not at all; 10=extremely helpful)	14	4.2	3.0
Q5. How much do you experience symptoms from your illness? (0=no symptoms at all; 10=many severe symptoms)	15	6.3	2.9
Q6. How concerned are you about your illness? (0= not at all concerned; 10= extremely concerned)	15	6.8	3.3
Q7. How well do you feel you understand your illness? (0=don't understand at all, 10=understand very clearly)	15	6.1	3.2
Q8. How much does your illness affect you emotionally? (0=not at all affected emotionally; 10=extremely affected emotionally)	15	6.9	2.9
Q9. List in rank order the three most important factors that you believe caused your illness	Factor 1	Factor 2	Factor 3
Case 1	Blocked ears	Vertigo	-
Case 2	Heart problem	Low BP	Head injury
Case 3	Labyrinthitis	-	-
Case 4	Anxiety	Poor hearing	Anger
Case 5	Grief	Depression	Anxiety
Case 6	-	-	-
Case 7	Gentamicin	-	-
Case 8	Stress	Tiredness	Migraines
Case 9	Viral infections	Labyrinthitis	Stress
Case 10	Head trauma	Disastrous life	-
Case 11	Mother's death	Father's cancer	Quit smoking
Case 12	Ménière's disease	-	-
Case 13	Labyrinthitis	-	-
Case 14	-	-	-
Case 15	Thunderclap headaches	Delay in BPPV treatment	-

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Figure 1.JPEG

