Coversheet

Title: Postural misperception: a biomarker for Persistent Postural-Perceptual Dizziness

Running head: Postural misperception in PPPD

Author names and degrees: Eduardo San Pedro Murillo PhD[1†], Matthew J. Bancroft PhD [2,3†], Nehzat Koohi PhD [2,4,5], Patricia Castro PhD[2,5], Diego Kaski PhD*[2,4,5]

Affiliations

[1]Department of Neurology, University Hospital "12 de Octubre", Madrid, Spain

[2]Centre for Vestibular and Behavioural Neuroscience, Department of Clinical and Movement Neurosciences, Institute of Neurology, University College London, London, UK

[3]Department of Brain Repair and Rehabilitation, University College London, Queen Square Institute of Neurology, London, UK

[4]The Ear Institute, University College London, London, UK

[5]Department of Neuro-otology, Royal National ENT and Eastman Dental Hospitals, University College London Hospitals, London, UK

[†] These authors contributed equally

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* Corresponding author address:

A/Professor Diego Kaski, Centre for Vestibular and Behavioural Neuroscience, Department of Clinical and Movement Neurosciences, UCL, 33 Queen Square, London WC1N 3BG

Tel: +44 20 3448 3135 Fax: +44 20 3448 4775 email: d.kaski@ucl.ac.uk

Abbreviations

PPPD Persistent Postural Perceptual Dizziness

BV Bilateral Vestibulopathy

ICVD International Classification of Vestibular Diseases

Introduction

Persistent Postural Perceptual Dizziness (PPPD) describes a persistent sensation of dizziness and/or unsteadiness (without vertigo) aggravated by upright posture that generates increased postural sway (1). Here we introduce a novel measure of perceived instability to investigate the relationship between observed sway and perceived instability in patients with PPPD compared to patients with persistent 'objective' instability due to bilateral vestibulopathy (BV).

Methods

Participants

Nineteen individuals with PPPD, according to the diagnostic criteria of the International Classification of Vestibular Diseases (ICVD) and 10 disease controls with bilateral vestibulopathy (confirmed with objective vestibular function testing), following informed consent. PPPD patients were randomly allocated to an 'intervention' (n=7) and 'no-intervention' group (n=12). Ten healthy controls were also recruited to validate the novel measure of perceived instability.

Measurement of Observed Sway

All participants performed 3 identical 20-second trials of quiet standing on a firm surface with eyes closed, arms by the sides, and feet together. Healthy controls stood on foam to increase instability.

Observed sway was measured using a force plate (EquiTest® or Kistler 9281C1, Winterthur, Switzerland) and quantified as the centre of pressure mean velocity, calculated as total horizontal distance travelled over the trial divided by time (20 seconds).

Measurement of Perceived Instability

Firstly, participants verbally rated their perceived instability during the observed sway measurements ("How unstable did you feel during the trial?") using a 0–10 ranked scale, where 0 corresponds to being "completely steady" and 10 "so unsteady that I would fall". Secondly, participants replicated their perceived instability by moving their body how they thought they were swaying during the observed sway measurements ("Move your body how you felt you were moving during the trial"). This perceived instability (herein termed 'reproduced' instability) was quantified by measuring sway whilst standing on the force plate with eyes open

but otherwise in an identical manner to the observed instability measurements (note healthy controls stood on foam for the observed but a firm surface for the reproduced instability measurement). We computed the observed:reproduced sway ratio for each individual and reasoned it should equal one if perceived instability was accurately replicated and our reproduced instability measure was valid.

Other Measurements

Participants completed two self-administered questionnaires: the State-Trait Anxiety Inventory scale (STAI-S) and the Dizziness Handicap Inventory (DHI).

Intervention

PPPD participants in the intervention group were shown a video recording of themself during the observed sway measurements, plus their centre of pressure trajectories. The discordance between perceived and actual sway was highlighted and an explanation for this in relation to PPPD given. The observed, perceived and reproduced instability measurements were then repeated.

Statistical Analysis

Group-level statistics are reported as medians and 25-75th quantile ranges. Statistical significance was set at $p<0.05$ after Bonferroni correction for multiple comparisons. Analysis was performed in Matlab 2021a (Mathworks, Natick, MA).

Results

There was no significant difference in age, gender distribution, height, dizziness handicap (PPPD: 64 [49-79]; BV: 50 [26-74]), or state anxiety (PPPD: 44 [29-59]; BV: 40 [29-51]) between patient groups ($p>0.05$ for all).

The relationship between observed and perceived instability differed in PPPD compared to BV (Fig 1A; $D(6.55)=0.684$, $p=0.003$). Observed sway tended to be less in PPPD than BV patients ($W=189$, $z=1.77$, $p=0.077$) but, despite this, PPPD patients perceived significantly greater instability than BV ($W=349.5$, $z=3.00$, $p=0.003$).

We then validated the reproduced instability measure on healthy controls and confirmed that reproduced sway was proportionate to observed sway (Fig 1D). Observed:reproduced sway was indistinguishable from a one-to-one relationship on average (ratio=1.11 [0.80-1.18]; ratio v one: $W=32$, $p=0.679$; i.e., ratio≈1; Fig 1F), showing that healthy controls could accurately replicate their perceived instability.

Generally, BV patients' reproduced sway closely matched observed sway, but PPPD patients over-reproduced observed sway (Fig 1B, C & E). Like healthy controls, reproduced sway was proportionate to observed sway in BV (ratio=1.09 [0.84-1.48]; ratio v one: $W=37$, $p=0.375$; i.e., ratio≈1; Fig 1E). PPPD patients' reproduced sway was on average double observed sway (ratio=2.01 [1.23-3.65]), which was significantly greater than both BV ($W=341$, $z=2.55$, $p=0.011$) and one ($W=185$, $z=3.62$, $p<0.001$).

The intervention altered the relationship between observed, perceived and reproduced instability in PPPD (Fig 1A,C,F insets). Observed sway did not change from pre- to post-intervention (paired difference: -0.03 [-0.3-0.05] cm/s; W=12, p=0.813). However, the intervention reduced both perceived instability (paired difference: 2.00 [1-4] points; W=21, p=0.031) and reproduced instability (paired difference: 3.3 [0.7-5.3] cm/s; W=28, p=0.016), and subsequently observed:reproduced ratio (paired difference: 1.00 [0.36-5.87]; W=28, p=0.016). Post-intervention reproduced sway was proportionate to observed sway in PPPD (ratio=1.04 [0.88-1.24]; ratio v one: W=16, p=0.813; i.e., ratio≈1) and ratio was no different from BV (W=61, p=0.887).

There were no significant correlations between perceived and reproduced instability for either patient group, nor between STAI, DHI and any other measure.

Discussion

The key finding was increased perceived instability in PPPD incongruent with observed sway (Fig 1A-C). Patients with 'objective' instability due to BV and healthy controls, made unstable by standing on foam, displayed perceived instability proportionate to actual sway. Our simple intervention suggests it is possible to reduce, at least transiently, the perception of sway in PPPD by providing visual feedback of a patient's actual sway. Future work should probe whether the intervention reduced instability scores or perception of instability.

The abnormal relationship between actual and perceived sway in PPPD represented an average 2-fold increase in sway misperception (Fig 1F). Such errors of magnitude estimation are coherent with abnormal threat assessment and bodily hypervigilance displayed by patients with PPPD following an acute episode of postural instability (2). Actual and perceived sway are proportionate in healthy individuals experiencing postural perturbation, but can be dissociated under conditions of postural threat (standing at height) (3). In contrast, PPPD patients have a disproportionate increase in the perception of sway relative to actual sway due perhaps to central alterations in magnitude estimates of self-motion signals (4). This thwarts normal readaptation to a postural threat event and actuates a vicious cycle of maladaptation (2).

Here, we capture the nature and magnitude of misperceived sway and argue that future biomarkers of PPPD may need to include measures of perceptual impairment, rather than relying on observed postural sway outcomes, where differences between patients with PPPD and even healthy controls are inconsistent (1, 5).

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Author Contributions

ESPM contributed to the conception and design of the study, acquisition and analysis of data and drafting of the manuscript. MJB contributed to the conception and design of the study, analysis of data and drafting of the manuscript and figures. PC contributed to acquisition and

analysis of data and drafting of the manuscript. NK contributed to acquisition of data and drafting of the manuscript. DK conceived the study and contributed to the acquisition and analysis of data and drafting of the manuscript and figures and approved the final version. All authors critically reviewed and approved of the manuscript.

Competing Interests

All authors report no competing interests.

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Figure Legends

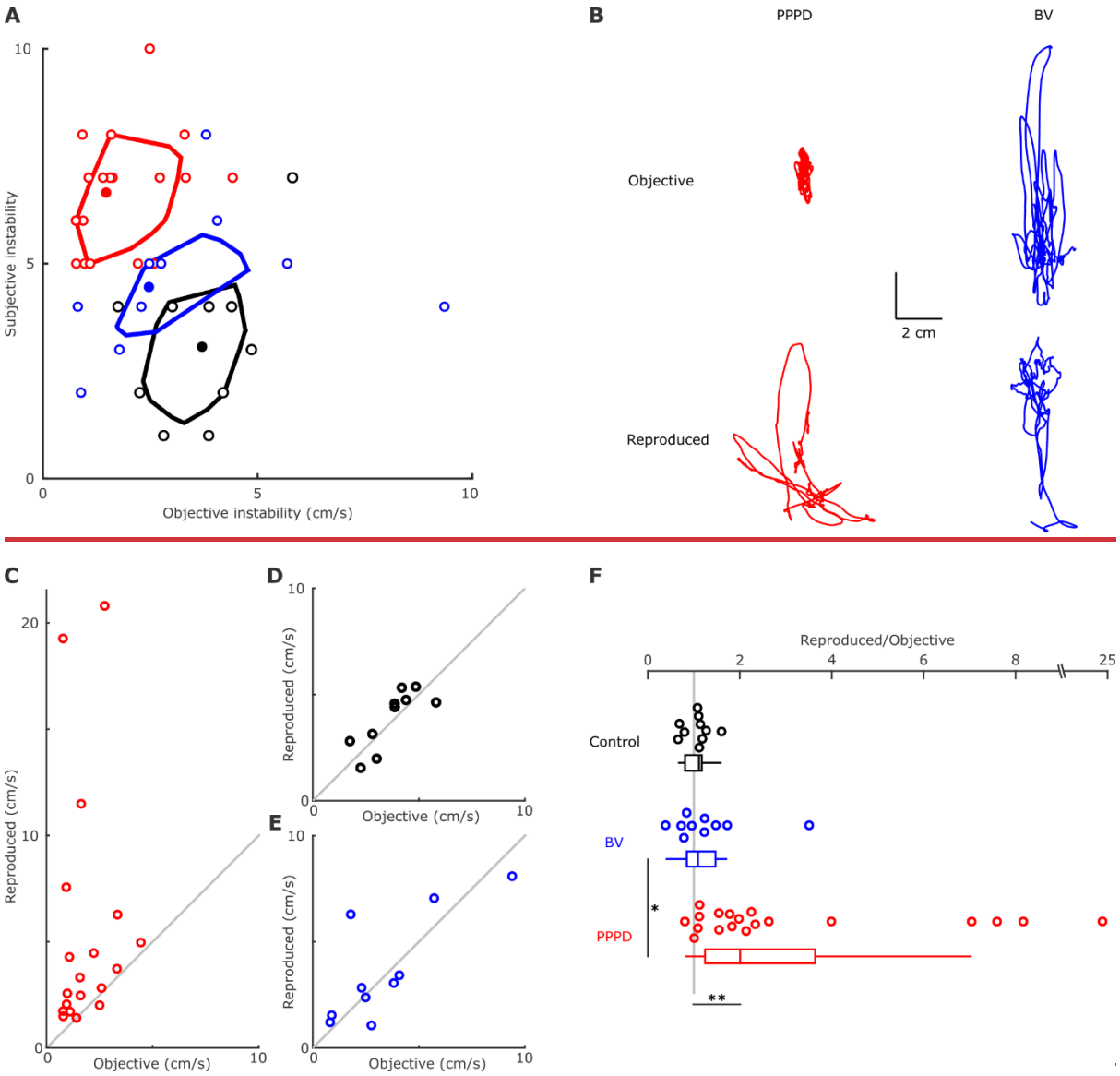

Figure 1. Observed sway versus perceived instability.

A: Bagplot of observed sway versus perceived instability for controls standing on foam (black), BV (blue) and PPPD patients (red). Unfilled circles are mean values for individual subjects. '+' are (Tukey's) group median values. The surrounding region ('bag') is the bivariate analog of the group interquartile range. Note lesser observed but higher perceived instability in PPPD compared to BV. Control data is shown for reference but was not statistically compared to PPPD and BV as controls performed the postural task on foam (to increase instability) and results are not directly comparable. B: Centre of pressure horizontal trajectories over a single 20 second recording of observed (top) and reproduced sway (bottom) for one PPPD (left) and BV (right) patient, matched for perceived instability, gender, age and height. Note the similarity between observed and reproduced sway in BV and the greater reproduced than observed sway in PPPD. C-E: Observed versus reproduced sway for controls standing on foam (black), BV (blue) and PPPD patients (red). The scale is identical in C-E and unfilled circles are mean values for individual subjects. F: Objective:reproduced sway ratio. Group data is summarised by box and whisker plots. In C-F grey lines represent where reproduced equalled observed sway (ratio=1).

Note that removal of the PPPD subject where ratio=24.9 in F does not affect group statistical differences. Insets within A, C & F show the effect of intervention on individual PPPD patients (pre: unfilled circles; post: filled circles; lines join individuals). *PPPD v BV or Pre v Post: $p<0.05$, **PPPD v one: $p<0.001$