1	Clinical Techniques and Technology: Vestibular Telemetry
2	Running title: Vestibular Telemetry
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16	Source of Funding:
17	John Phillips takes full responsibility for the integrity of the content of this manuscript. This work
18	was supported by the UK Medical Research Council under Grant MR/P026265/1.
19	
20	Author Contributions:
21	JP – project conception and design, data collection, analysis and write up. JN – project design, data
22	collection, analysis and write up. SC – project conception and design, analysis and write up.
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24	Declaration of Interest Statement:
25	All three authors are listed as inventors on a patent application for the CAVA® device, filed by the
26	University of East Anglia.

27 Abstract

29	When a patient presents to a clinician with dizziness, it can be difficult for the patient to describe
30	their symptoms in a clear manner, and clinical examination often yields entirely normal results.
31	Ideally, it would be favourable to measure key physiological parameters during their episodes of
32	dizziness. From a clinical perspective, this would allow a more timely and more accurate diagnosis.
33	From a research perspective, it would allow a greater understanding of how the vestibular system
34	malfunctions as a consequence of vestibular disease. The authors of this report have been funded
35	by the UK Medical Research Council to develop and test novel technology to measure, record and
36	analyse key physiological parameters provided by the dizzy individual during episode of dizziness
37	whist active in the community. We provide the context to evolving work in this field, the outcome of
38	preliminary studies and a consideration of future opportunities.
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41	Keywords
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43	Ménière's Disease; Migraine; Benign Paroxysmal Positional Vertigo, Nystagmus, Dizziness, Vestibular
44	Diseases.
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48 Introduction

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50 Dizziness is a common complaint that places a significant burden on health services worldwide.<sup>1</sup> 51 Dizziness affects 20–50% of individuals during their lives and up to 10% of affected individuals 52 experience vertigo.<sup>2</sup> In 80% of affected individuals, vertigo results in a medical consultation, 53 interruption of daily activities, or sick leave.<sup>3</sup> 54 55 56 Vestibular telemetry 57 58 Contemporary methods to evaluate the dizzy patient only provide a snapshot of vestibular function 59 when performed in the absence of a 'dizzy attack'. Nystagmus is a key clinical sign that should be 60 documented when assessing patients with vertigo and various patterns of nystagmus are produced 61 as a consequence of different disease processes. If it were possible to continuously monitor dizzy 62 patients in the community, the presence of a nystagmus pattern could aid diagnosis. We term this 63 diagnostic process, 'vestibular telemetry'. This approach is analogous to the 24-hour ECG tape used 64 to identify cardiac arrhythmias. 65 66 67 The CAVA system 68 69 The CAVA (Continuous Ambulatory Vestibular Assessment) system consists of a wearable device and 70 computer algorithms to identify nystagmus. The device includes a single-use sensor array that 71 adheres to the face to capture horizontal and vertical eye-movements, and a reusable module 72 containing an accelerometer, microcomputer, data storage, battery, and connection port (Figure 1). 73 Eye-movements are recorded via the corneo-retinal potential generated by the eyes. A sampling

rate of 42 Hz is used; close to a typical lower-end for videonystagmography. This rate reconciles data
storage requirements against the level of resolvable detail. Device calibration is not required to
identify nystagmus, but an average calibration value is assumed when calculating slow phase
velocities.

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The CAVA device was developed to allow continuous recording of eye and head movements for 23 hours a day, for 30-days, in the community. Patients remove the device each morning for an hour and then reapply it to themselves. The following findings were obtained from two clinical investigations which were reviewed and approved by the NHS Health Research Authority's London-Dulwich Research Ethics Committee (IRAS: 261099 and 240847).

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We initially tested the CAVA system on a group of healthy individuals to evaluate the suitability of 85 86 the device, and our algorithms' accuracy at detecting nystagmus induced using an optokinetic video 87 stimulus viewed on a mobile phone.<sup>4</sup> The algorithms detect the presence of nystagmus using a novel 88 combination of machine learning techniques, and then bespoke analysis routines quantify its more 89 detailed characteristics.<sup>5</sup> The CAVA system consistently, precisely and reliably identified periods of 90 induced nystagmus in both stationary and moving subjects with a sensitivity and specificity of 99.1% 91 (95% CI: 95.13% to 99.98%) and 98.6% (95% CI: 96.54% to 99.63%), respectively. The system could 92 also identify the frequency and beat direction of nystagmus.<sup>5</sup>

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Other technologies have been developed to monitor dizziness in the community but have suffered from fundamental limitations, prohibiting continuous wear due to limited data storage, insufficient portability and inadequate battery life. The CAVA device is small enough to be worn for thirty days, stores more than a month's worth of data, and requires a single battery change after fifteen days. Technologies employing videonystagmography require the eyes to remain open, but patients often close their eyes during vertigo and while asleep. Devices requiring donning or activation upon the

100 onset of dizziness rely on having the device to hand and being physically capable of doing so;

101 challenging for elderly individuals or those experiencing severe symptoms.

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## 104 **Clinical Applications**

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106 We are currently investigating the applicability of the CAVA system in patients reporting vertigo. We 107 have identified quantifiable differences between the nystagmus produced by our target conditions: 108 Ménière's disease, vestibular migraine and Benign Paroxysmal Positional Vertigo (BPPV).<sup>6</sup> Figures 2 109 to 4 show nystagmus traces produced by these conditions. We have discovered that nystagmus 110 produced during an attack of Ménière's disease occurs in short episodes lasting several hours, during 111 which the "beat" direction alternates in relation to the affected ear.<sup>7</sup> By contrast, nystagmus during 112 a vestibular migraine attack is shorter in duration and its slow phase velocities are generally lower. 113 The nystagmus of BPPV is even shorter in duration and is induced by acceleration of the head, as 114 confirmed by CAVA's accelerometer signals. 115 116 We have recorded an entire episode of vertigo in a patient with Ménière's disease.<sup>7</sup> Because we 117 recorded eye movements before, during and after the attack, we have discovered a possible 118 prodromal phase. If this is a consistent feature of Ménière's disease, it could be exploited to warn 119 patients of an impending attack. In another study, we analysed nystagmus traces from different 120 patients with Ménière's disease, revealing how the characteristics of nystagmus could aid decision 121 making with respect to treatment.<sup>8</sup> 122 123 124 **Future developments** 

126	The CAVA system fulfils an unmet clinical need to provide a long-term, objective record of a patient's
127	vertigo. Such a record could also be used to confirm reports of 'dizziness' following work-related
128	head injuries or road accidents. The CAVA device has the potential to aid the diagnosis and
129	understanding of many areas of vestibular medicine, conditions outside the vestibular system, non-
130	vestibular areas of medical research (e.g. sleep medicine), and beyond (e.g. driver alertness
131	monitoring).
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133	The diagnosis of Ménière's disease and vestibular migraine is contentious. Many tests are often
134	required, including radiological investigations, audiometry and other specialist vestibular tests. As
135	more nystagmus data become available, in addition to identifying nystagmus patterns that are
136	consistent with conditions such as Ménière's disease and vestibular migraine, it might be possible to
137	create universal diagnostic criteria for these conditions, as well for disease subtyping, grading and
138	staging.

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141	References				
142					
143	1.	Kovacs E, Wang X, Grill E. Economic burden of vertigo: a systematic review. Health Econ Rev.			
144		2019; 9. DOI: https://doi.org/10.1186/s13561-019-0258-2			
145					
146	2.	Teggi R, Manfrin M, Balzanelli C, et al. Point prevalence of vertigo and dizziness in a sample of			
147		2672 subjects and correlation with headaches. Acta Otorhinolaryngol Ital. 2016;36(3):215-			
148		219. DOI: https://doi.org/10.14639/0392-100X-847			
149					
150	3.	Neuhauser HK, von Brevern M, Radtke A, Lezius F, Feldmann M, Ziese T, Lempert T.			
151		Epidemiology of vestibular vertigo: a neurotologic survey of the general population.			
152		Neurology. 2005 Sep 27;65(6):898-904. DOI:			
153		https://doi.org/10.1212/01.wnl.0000175987.59991.3d			
154					
155	4.	Phillips JS, Newman JL, Cox SJ. An investigation into the diagnostic accuracy, reliability,			
156		acceptability and safety of a novel device for Continuous Ambulatory Vestibular Assessment			
157		(CAVA). Scientific Reports. 2019;9(1):10452.			
158					
159	5.	Newman JL, Phillips JS, Cox SJ. Automatic nystagmus detection and quantification in long-term			
160		continuous eye-movement data. Comput Biol Med. 2019:103448.			
161					
162	6.	Phillips JS, Newman JL, Cox SJ. Towards providing an automated approach to differentiating			
163		the nystagmus of Ménière's Disease, Vestibular Migraine and Benign Paroxysmal Positional			
164		Vertigo. Otol. Neurotol. 2020 (In Press)			

- 165 7. Phillips JS, Newman JL, Cox SJ, FitzGerald JE. Nystagmus during an acute Ménière's attack:
- 166 from prodrome to recovery. *International Journal of Audiology*. 2020. DOI:

167 <u>10.1080/14992027.2020.1799252</u>

- 168
- 169 8. Phillips JS, Newman JL, FitzGerald JE, Cox SJ. Implications of vestibular telemetry for the
- 170 management of Ménière's Disease—Our experience with three adults. *Clin Otolaryngol*. 2020.
- 171 DOI: <u>https://doi.org/10.1111/coa.13676</u>

172 Figures

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174 **Figure 1:** The CAVA device. Two electrodes either side of the eyes record horizontal eye movement,

- 175 two above and below one eye record vertical eye movement, and a fifth beneath the right ear
- 176 provides a reference voltage.

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178 **Figure 2:** Left-beating nystagmus during an attack of Ménière's Disease. Fast/slow phases are shown

179 in red/green. The attack occurred over about three hours and consisted of eight separate episodes

180 of nystagmus.

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182 **Figure 3:** Right-beating nystagmus during a vestibular migraine attack. Fast/slow phases are shown

183 in red/green. Compared to Figure 2, slow phase durations are longer and slow phase velocities are

184 lower. The attack lasted about an hour.

- 186 **Figure 4:** Nystagmus during a BPPV attack. This nystagmus is oscillatory without obvious fast or slow
- 187 phases (red boxes). After starting, the nystagmus briefly subsided before resuming again. The
- 188 duration of the nystagmus was approximately twenty seconds.