

## 1 Introduction

2

3 Dizziness is an extremely common symptom. One survey showed that over 20% of 18 to 64  
4 year olds registered at four GP surgeries in London had experienced dizziness within the  
5 preceding month.<sup>1</sup> Patients with vertigo can experience violent spinning episodes for hours  
6 at a time.<sup>2</sup> Vertigo can have many causes, and although a wide range of clinical tests are  
7 available, they are often undertaken in the absence of a dizzy attack.<sup>3</sup> Furthermore, patient  
8 reporting of vertigo is subjective and imprecise.<sup>4</sup> Therefore, dizziness can be challenging to  
9 diagnose and it would be beneficial to diagnose patients quickly and accurately, reducing  
10 the burden on health services.

11

12 Observation of eye movements is informative when assessing the dizzy patient. Vertigo is  
13 usually accompanied by nystagmus, and different patterns of nystagmus can help provide a  
14 diagnostic insight into the underlying cause of a patient's symptoms.<sup>5,6</sup> For example,  
15 nystagmus beating in the horizontal plane is often characteristic of problems in the inner  
16 ear, whereas nystagmus in the vertical plane can be suggestive of central causes.<sup>7</sup> We have  
17 developed the Continuous Ambulatory Vestibular Assessment (CAVA<sup>®</sup>) device to provide  
18 valuable long-term eye movement data (Figure 1), and computer algorithms for analysing  
19 the data collected by the device in the community. As with conventional  
20 electronystagmography, the CAVA<sup>®</sup> device records horizontal and vertical eye-movements  
21 but does not capture torsional eye-movement data. This system provides an objective  
22 record of the presence, duration and frequency of nystagmus, gathered over a period of  
23 thirty days.

24

25 The CAVA<sup>®</sup> system has proven capable of detecting induced nystagmus and nystagmus in  
26 patients suffering from a variety of vestibular conditions.<sup>8-11</sup> The long-term data captured  
27 can provide an objective record of the presence of nystagmus, which patients are unlikely to  
28 report accurately by themselves. We have previously shown that nystagmus during a  
29 Ménière's attack has unique temporal characteristics, which could be used to assist in  
30 diagnosing the condition.<sup>10</sup> Other conditions, such as Benign Paroxysmal Positional Vertigo  
31 (BPPV), are distinct in that they are motion-provoked, and nystagmus is short in duration.  
32 BPPV from nystagmus typically beats torsionally and vertical upwards, although only the

33 vertical component can be detected by the CAVA<sup>®</sup> system. The information provided by the  
34 CAVA<sup>®</sup> system is expected to supplement and complement a full neurological history and  
35 examination, assisting the clinician to make or confirm a diagnosis.<sup>11</sup>

36

37 The large quantity of data captured by the device makes manual inspection of the data  
38 impractical. To overcome this issue, we have previously developed and evaluated  
39 algorithms to automatically detect different patterns of nystagmus,<sup>9</sup> for subsequent review  
40 and interpretation by a clinician. Eye movement data can be difficult to interpret from  
41 manual inspection of separate vertical and horizontal channels, especially if the eye  
42 movements are complex or rare.<sup>12</sup> Additionally, some clinicians may have more experience  
43 examining the eyes than looking at signal traces. Patients themselves would better  
44 understand their own symptoms from a video representation of their eye-movements  
45 rather than complex signal traces. In this article, we describe an approach to reproduce  
46 animated eye movements from the long-term, horizontal and vertical electrooculography  
47 data provided by the CAVA<sup>®</sup> device. The recreated movements imitate the appearance of  
48 the eyes, excluding torsional eye-movements, and largely allowing clinicians to review  
49 episodes of vertigo as if they were present with the patient during an attack. We  
50 demonstrate that the results obtained are visually comparable to actual video footage of  
51 the patient's eyes. The data analysed exemplifies the challenges associated with  
52 interpreting eye-movement signals and highlights the benefits of reanimating them in 2D.

53

## 54 **Materials and Methods**

55

56 We are currently undertaking a clinical investigation into the capabilities of our device to  
57 detect pathological nystagmus from patients with a range of vestibular conditions. This  
58 work is part of a larger portfolio of work funded by the UK Medical Research Council to  
59 develop a full medical system for diagnosing dizziness. During the "training" phase of this  
60 investigation, we have collected data from patients with vertigo which will be used to  
61 develop our computer algorithms for detecting nystagmus. The work presented here was  
62 undertaken using data from patients enrolled onto this training phase. This clinical  
63 investigation was reviewed and approved by the London-Dulwich Research Ethics  
64 Committee (IRAS Number: 261099)

65

66 Patients enrolled into our clinical trial wore the CAVA<sup>®</sup> device for thirty consecutive days.  
67 They attended three separate follow-up appointments during the trial. The first, on day five,  
68 was to check that the patient was getting on well with their device and to check for adverse  
69 skin reactions. The second, on day fourteen, was to change the device's battery. After day  
70 thirty-one, patients returned their device and completed a questionnaire. In this article, we  
71 present data from two of the trial participants. Patient One was a 53-year-old lady with a  
72 fifteen-year history of left-sided unilateral Ménière's disease. Patient Two was a 56-year-old  
73 lady with a three-year history of positional vertigo. For Patient One, we reanimated her  
74 nystagmus eye movements from a Ménière's attack she experienced during her thirty-day  
75 trial, in her own home. For Patient Two, we reanimated her nystagmus during a Dix-Hallpike  
76 test, undertaken in a clinical setting at her day fourteen follow-up appointment. We also  
77 recorded concurrent video footage of Patient Two's eyes during this test. The video was  
78 recorded using a Canon 200D Digital SLR camera, at 1920 x 1080 pixels, at 60 frames per  
79 second.

80

81 The CAVA<sup>®</sup> device (Figure 1) records the corneo-retinal potential produced by the eyes,  
82 which is a proxy for eye movement. Horizontal eye movement is captured by way of two  
83 electrodes placed at the outer canthi of the eyes, and vertical eye movement by two  
84 electrodes placed above and below the left eye. A fifth electrode beneath the right ear  
85 provides a reference voltage. This technology is similar to electrooculography and  
86 electronystagmography, which have been used routinely for decades,<sup>13</sup> and as such the  
87 CAVA<sup>®</sup> device does not capture torsional eye-movements. Also, as with  
88 electronystagmography, the CAVA<sup>®</sup> device would require frequent recalibration in order to  
89 relate the signals recorded to precise eye-movements in degrees. As we are presently only  
90 interested in identifying nystagmus signals and comparing them qualitatively, here we  
91 present eye-movements using native device units. The device also contains an  
92 accelerometer which records three-axis head movements. Each channel of eye movement is  
93 sampled at 42.67 Hz and each acceleration channel is sampled at 20 Hz.

94

95 We developed software to simultaneously visualise the two-channel eye-movement data  
96 provided by the CAVA<sup>®</sup> device, the video data (for Patient Two), and a 2D reconstructed

97 animation of the patients' eye movements. This software, which was created using  
98 Mathwork's MATLAB, generates a video file showing the three modalities playing in real-  
99 time: vertical and horizontal eye-movement traces, an animated reconstruction of the eyes  
100 and concurrent video footage of the patient's eyes. Prior to visualisation and reconstruction,  
101 each eye movement channel was pre-processed to remove signal drift and high frequency  
102 noise, such as interference from mains electricity, both common issues when working with  
103 electrooculography data.<sup>14</sup> To achieve this, a bandpass filter was applied to the data (Figure  
104 2). The filter used a high-pass threshold of 0.20 Hz and a low-pass threshold of 6 Hz.

105

106 Animated eye-movements were reconstructed by plotting the filtered horizontal and  
107 vertical eye-movement channels onto two separate 2D plots, designed to imitate the  
108 appearance of the pupils of the eyes. Although the CAVA<sup>®</sup> device does not record left and  
109 right eye movements independently, both eyes are shown in order to generate a more  
110 realistic and interpretable animation. The axes limits of the reconstructed plots were  
111 selected such that all of the patient's eye-movement data would be visible within the plots.  
112 The video data was temporally aligned with the eye-movement data using activation of the  
113 CAVA<sup>®</sup> device's event marker as a reference point. As the device and video data were  
114 captured at different sample rates, care was taken to maintain alignment of these data  
115 channels during playback.

116

## 117 **Results**

118

119 Patient One returned their device after thirty days and reported an acute Ménière's attack  
120 consisting of an episode of rotary vertigo lasting approximately three hours. Analysis of the  
121 eye-movement traces from the CAVA<sup>®</sup> device showed clear evidence of sporadic, left- and  
122 right-beating jerk nystagmus throughout the period indicated by the patient. The full details  
123 of this attack have been reported previously.<sup>10</sup> A thirty-second extract of the device data  
124 was processed by our software to generate a new video showing the horizontal and vertical  
125 eye-movement traces alongside a 2D-reconstruction of the patient's eye movements (Figure  
126 3 and Supplemental Movie 1). The reconstruction confirmed the presence of right-beating,  
127 jerk nystagmus during the reported vertigo attack.

128

129 Patient Two returned after thirty days, reporting several short episodes of motion-provoked  
130 vertigo during the trial. At Patient Two's second follow-up visit, three right-sided Dix-  
131 Hallpike manoeuvres were performed. Visual observation of the patient's eyes during these  
132 tests showed nystagmus beating torsionally with the upper pole of the eye to the right-hand  
133 side, and vertically upward. The nystagmus lasted for less than thirty seconds. These  
134 observations confirmed right posterior canal, BPPV canalithiasis. Consistent with the  
135 response "fatigue" that has been reported previously, the first manoeuvre yielded the  
136 strongest nystagmus response.<sup>15</sup> To compare the patient's actual eye-movements with  
137 those recreated from the device data, we recorded video of the patient's eyes whilst they  
138 underwent the manoeuvre. The video and device data were processed by our software to  
139 generate a new video showing these modalities alongside a 2D-reconstruction of the  
140 patient's eye movements (Figure 3 and Supplemental Movie 2). Observation of the CAVA®  
141 device's horizontal and vertical eye movement data showed evidence of up-beating  
142 nystagmus in the vertical channel (Figure 3a-b).

143

144 The 2D animated reconstruction of Patient Two's eye-movements revealed an obvious  
145 visual correlation between the reconstruction and the video footage (Figure 3c and 3d). At  
146 about 00:13:36, the patient can be seen to blink (Figure 3d), and this appears as a fast,  
147 upward eye excursion in both the eye movement traces (Figure 3a-b) and the  
148 reconstruction (Figure 3c). From the reconstruction, Patient Two's eyes can also be seen to  
149 move in an arching motion towards the right-hand side of her face. This motion could not  
150 easily be identified from the eye-movement traces alone, but is clearly visible both in the  
151 reconstruction and in the video footage. As purely torsional eye-movements cannot be  
152 captured using electrode-based electronystagmography, no torsional movements are visible  
153 in the reconstruction, despite being visible in the video footage. The device's accelerometer  
154 data confirmed that the patient underwent a right-sided Dix-Hallpike test. Both the  
155 reconstruction and the video showed clear evidence of nystagmus starting approximately  
156 seven seconds after the patient was placed into a supine position, which lasted for  
157 approximately nine seconds. Up-beating nystagmus is visible in the vertical channel and the  
158 trace has an oscillatory appearance. After the nystagmus had subsided, the patients' eyes  
159 were visibly stationary.

160

161 **Discussion**

162

163 The results presented here have provided proof-of-concept that signals captured by the  
164 CAVA® device largely reflect the actual eye-movements displayed by patients. We were able  
165 to use reconstructed animated eye movements to observe the up-beating component of  
166 nystagmus present in a patient undergoing a Dix-Hallpike manoeuvre and also the jerk  
167 nystagmus experienced by a patient experiencing an attack of Ménière's disease, in her own  
168 home. In the absence of a video recording of a patient's eyes or without being physically  
169 present with a patient during a vertigo attack, an animated 2D reconstruction would enable  
170 clinicians to retrospectively evaluate the presence and characteristics of nystagmus, and  
171 would aid discussions with the patient regarding their vertigo. Clinicians may favour the  
172 animated 2D reconstruction because they are familiar with observing physical eye  
173 movements, or as highlighted here, because of the complexity of the signal under  
174 interrogation.

175

176 This study is the first to recreate eye-movements from the long-term data provided by the  
177 CAVA® device for the purpose of assessing dizziness. Due to the emergence of  
178 videonystagmography technology, electrooculography has decreased in popularity for  
179 recording nystagmus in clinical settings.<sup>16</sup> Interpreting eye movements from  
180 electrooculography (EOG) data remains an active area of research in the field of Human-  
181 Computer-Interaction (HCI). Applications of EOG in HCI tend to focus on the automatic  
182 detection of specific eye-movement gestures to facilitate some kind of computer-based  
183 activity, often to assist people with quadriplegia to interact with a computer.<sup>17</sup>

184

185 There is a clear similarity between the data captured by the CAVA® device and the actual  
186 eye-movements experienced by patients. This relationship is sufficient to allow a qualitative  
187 comparison between nystagmus from different patients and between nystagmus resulting  
188 from different conditions. There are several issues which make discriminating the  
189 characteristics of nystagmus more challenging. As with ENG, the relationship between eye-  
190 movements and native device units is only linear up to  $\pm 30$  degrees.<sup>18</sup> This is an  
191 unavoidable limitation of electrode-based systems, so care should be taken when visualising  
192 large excursions of the eye. It is also not possible to record pure torsional eye-movements

193 using electrode-based systems. Such eye-movements are common with BPPV, although they  
194 are usually accompanied by a vertical component.

195

196 A further challenge shared with conventional electrode-based electronystagmography is  
197 that frequent device calibration is usually required to determine precise eye-movements in  
198 degrees. This is due to the variability of the Corneo-Retinal Potential (CRP), which is the  
199 bioelectrical signal used by both systems as a proxy for eye-movement. Calibration can be  
200 performed by the subject performing a calibration task, such as predefined eye movements  
201 (e.g. moving the eyes by  $\pm 30$  degrees), in order to calculate the number of native device  
202 units per degree of eye movement. Alternatively, an average calibration value could be  
203 used, with a known margin of error. We did not perform these steps here as it is possible to  
204 determine the presence of nystagmus, its duration and beat-direction without prior  
205 calibration.

206

207 BPPV is the most common cause of vertigo, and by far the most common cause of motion-  
208 provoked vertigo. Thus, nystagmus correlated with head-movements, as confirmed by the  
209 CAVA<sup>®</sup> device's accelerometer data, would provide a likely first indication of BPPV. Further  
210 supporting data is provided by the fact that the onset of nystagmus is delayed for BPPV but  
211 not for vertigo with central causes, and the nystagmus produced as a consequence of BPPV  
212 is fatigable whereas for central causes it is not. Posterior canalithiasis is the most common  
213 form of BPPV, accounting for around 90% of cases. Therefore, in the majority of cases, the  
214 side the person lies on would indicate the affected side and the affected canal. Confirmation  
215 of motion-provoked vertigo fulfilling these criteria could be used in conjunction with a full  
216 neurotological history and examination to supplement a clinician's diagnosis.

217

218 We have shown here that eye blinks are reconstructed as short duration, vertical eye  
219 movements, which could be misinterpreted as genuine, vertical eye-movements. Some  
220 vertical movement can occur during blinking (Bell's phenomenon), but this is unlikely to fully  
221 account for the signals captured.<sup>19</sup> In light of this, it could be useful to develop ways to  
222 automatically detect blinks in the data, to alert the clinician of their presence.

223

224 The method of reconstructing eye movements presented here provides an alternative  
225 representation of the data captured by the CAVA<sup>®</sup> device, allowing easier interpretation of  
226 the patient's eye movements and confirming the presence of nystagmus to a clinician. Our  
227 ultimate goal is to further develop this system from one that detects nystagmus to one that  
228 can provide useful insights regarding the nature of the nystagmus detected. If deployed into  
229 routine medical care, we expect that the CAVA<sup>®</sup> system would be provided to patients in  
230 secondary care settings, most likely to provide an objective confirmation of vertigo and to  
231 aid the discrimination of possible vestibular causes. The system could provide insight into  
232 conditions with a degree of overlap, such as Ménière's disease and vestibular migraine, or  
233 for patients with coexistent conditions, such a dual diagnosis of BPPV and Ménière's  
234 disease. A combination of a full neurotologic history, examination and the nystagmus  
235 recorded over thirty-days would then guide a clinician towards the most likely diagnosis and  
236 treatment options. For example, hearing loss combined with prolonged episodes of  
237 direction-changing vertigo might suggest Ménière's disease. Prolonged nystagmus in the  
238 vertical plane might suggest a central cause. BPPV might be suggested by short durations of  
239 up-beating nystagmus, with a latency following a provocative head-movement, and this  
240 would be confirmed by a Dix-Hallpike test. As we work towards this goal, we next intend to  
241 undertake a clinical trial to determine whether the nystagmus signals captured by the  
242 CAVA<sup>®</sup> device are sufficient by themselves to differentiate some of the most common inner-  
243 ear causes of vertigo.

244

#### 245 **Declaration of Interest Statement**

246

247 All three authors are listed as inventors on a patent application for the CAVA<sup>®</sup> device.

248

#### 249 **Data Availability Statement**

250

251 The data presented here is available upon reasonable request.

252

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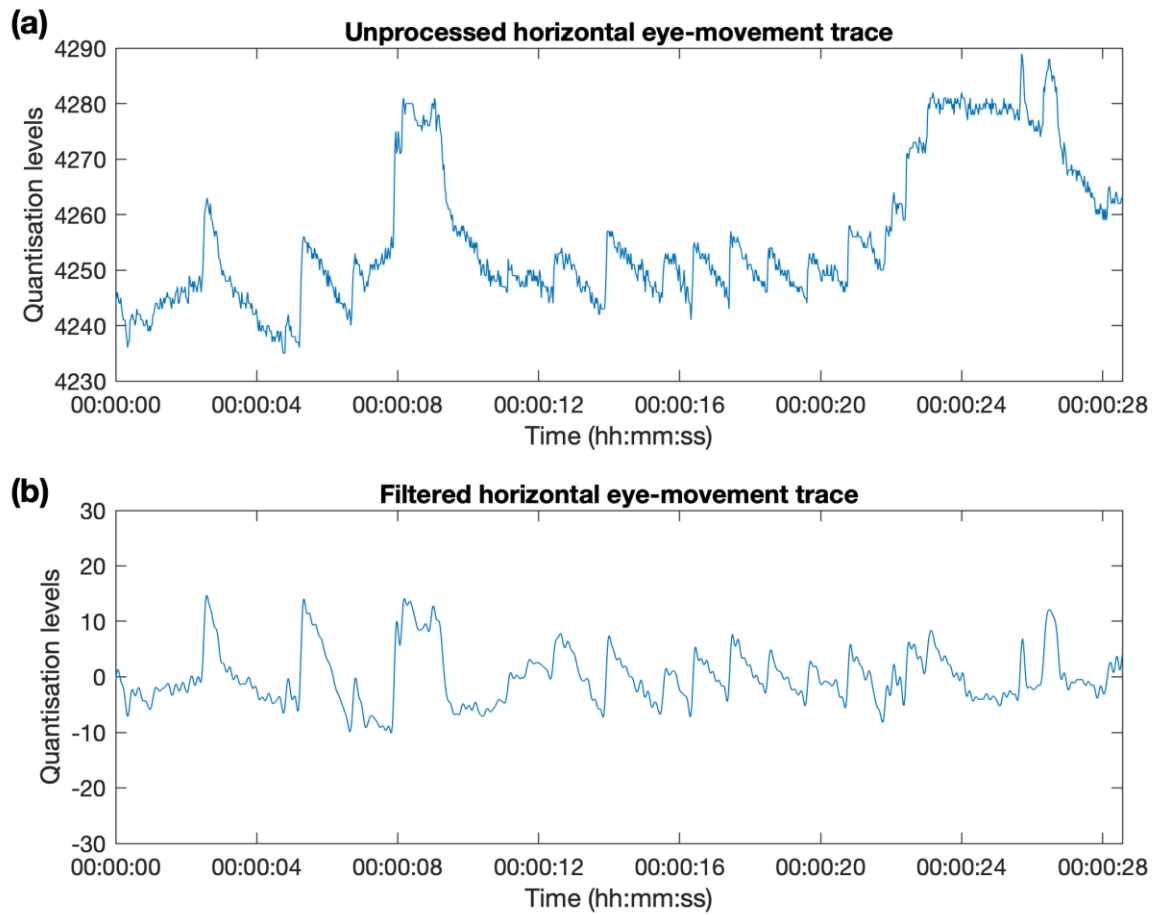
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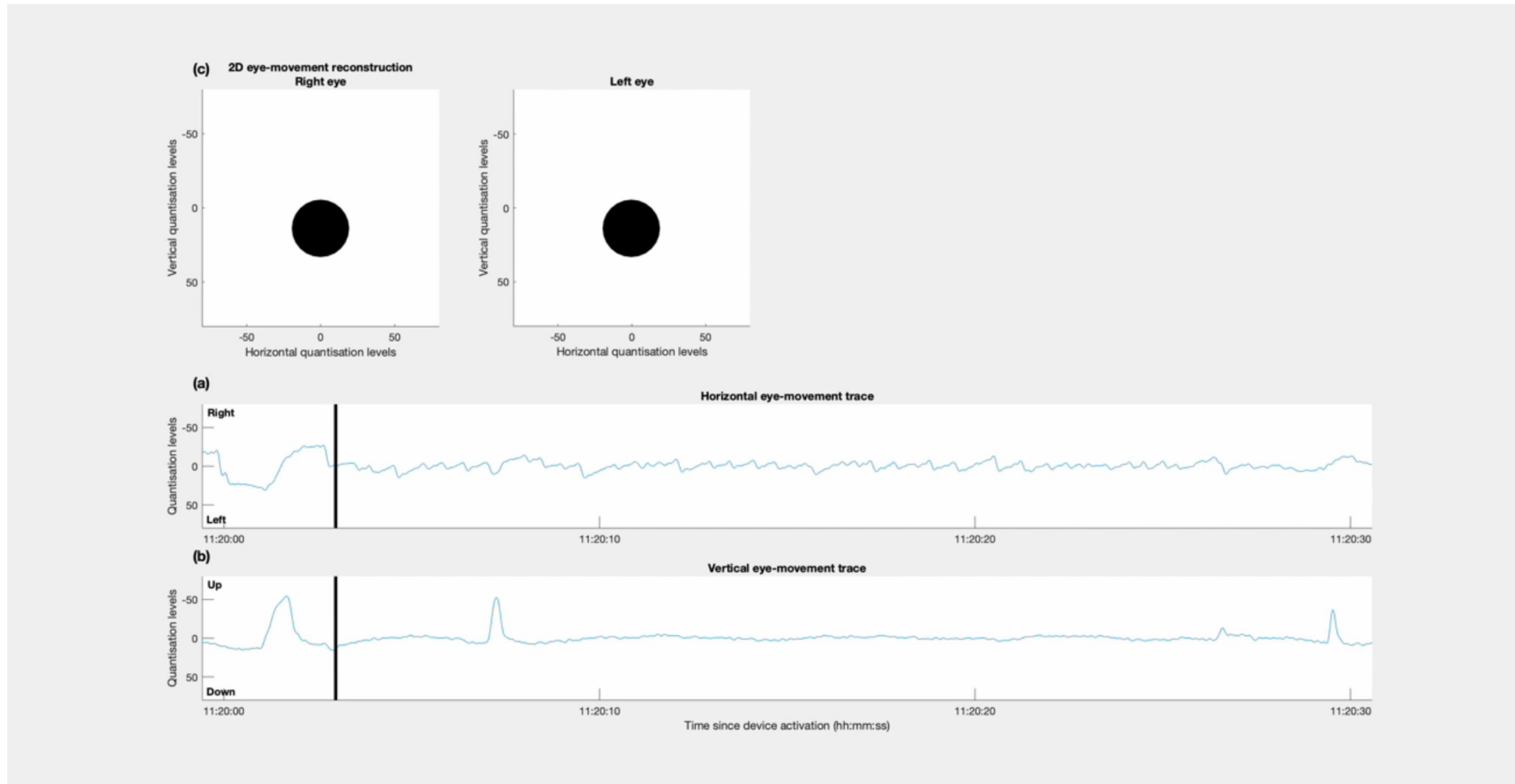
311 **Figure 1**

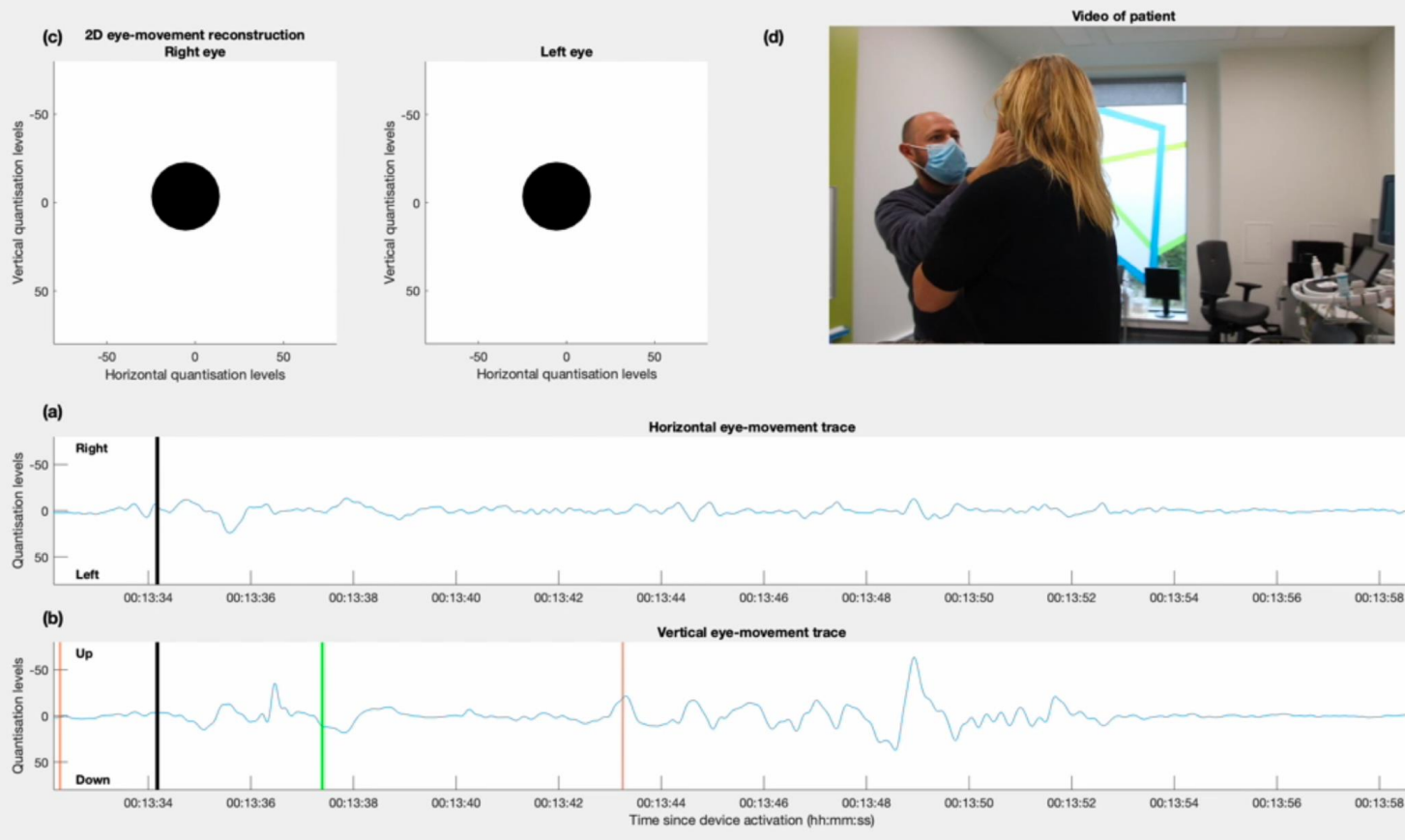
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313

314 **Figure 2**





318

319 **Figure 4**

320 **Figure 1:** The appearance of the CAVA<sup>®</sup> device when worn on the head. The device includes  
321 a reusable logging module and two, single-use electrode mounts. Five ECG electrodes are  
322 placed at specific sites on the face to record the corneo retinal potential produced by the  
323 eyes. A button on the logging unit allows the patient to activate the device's event marker,  
324 which causes the device to log the date and time of the button press. The button can also be  
325 used to initiate a status check of the device, the results of which are confirmed visually by  
326 the device's status LED. The status checking feature provides feedback regarding battery  
327 level, the connection of the device's electrodes, and confirmation of event marker  
328 activation.

329

330 **Figure 2:** Panels (a) and (b) display a 28-second, horizontal eye-movement trace captured by  
331 the CAVA<sup>®</sup> device. The waveforms show an extract of nystagmus produced by a patient with  
332 Ménière's disease. In panel (a), the signal has not been filtered, and shows evidence of  
333 signal drift and high frequency noise. In (b), the signal has been filtered using a bandpass  
334 filter, with a passband of 0.20 Hz to 6 Hz. The filtered signal retains the characteristic  
335 *sawtooth* nystagmus waveform shape whilst discarding the signal drift and the higher  
336 frequency noise.

337

338 **Figure 3:** The initial frame of a video showing the eye-movements of a patient experiencing  
339 an acute attack of Ménière's disease. The signal shown is an extract from an attack which  
340 lasted for approximately three hours, in total. (a) and (b) show the horizontal and vertical  
341 eye movement traces as captured by the CAVA<sup>®</sup> device. The black line marks the current  
342 timestamp. (c) Shows the animated reconstruction of the eye movements in 2D.

343

344 **Figure 4:** The initial frame of a video showing the eye-movements of a patient undergoing a  
345 Dix-Hallpike manoeuvre. (a) and (b) show the horizontal and vertical eye movement traces  
346 as captured by the CAVA<sup>®</sup> device. The black line marks the current timestamp, and event  
347 marker activations are shown as orange lines. (c) Shows an animated reconstruction of the  
348 patient's eye movements in 2D. The video in (d) shows the clinician activating the device's  
349 event marker, performing the Dix-Hallpike manoeuvre on the patient, followed by a closeup  
350 of the patient's eyes. The first event marker activation allowed the eye-movement channels  
351 to be aligned temporally with the video of the patient undergoing the procedure. The

352 second activation was at the first sign of nystagmus, which coincided with the patient  
353 reporting the onset of vertigo, and the final event mark was deployed after the nystagmus  
354 had ceased. The green line in (b) is the point at which the video in (d) is rotated by 180  
355 degrees, so that they are presented in the same orientation.