Objective: The diagnosis of vertigo is challenging, particularly as patients usually present whilst asymptomatic. We have developed an ambulatory medical device that allows vestibular telemetry to record eye movements over a 30-day period to aid the diagnosis of vertigo. We have undertaken proof-of-concept work to identify unique properties of nystagmus that could be used to differentiate between three of the most common causes of vertigo: Ménière's Disease, vestibular migraine, and Benign Paroxysmal Positional Vertigo.

Patients: We analyse the nystagmus from patients with a diagnosis of Ménière's Disease, vestibular migraine, and Benign Paroxysmal Positional Vertigo.

Intervention(s): Our vestibular telemetry system includes a wearable, ambulatory monitor which continuously records horizontal and vertical eye-movements, as well as 3-axis movements of the head.

Main Outcome Measure(s): Horizontal and vertical eye-movement data, and 3-axis head positioning data.

Results: Sixteen participants were enrolled onto the study and three reported experiencing rotatory vertigo during their thirty-day trial, confirmed by the presence of nystagmus in their eye-movement traces. Vestibular telemetry revealed distinct differences between the nystagmus produced during an acute Ménière's attack, and attacks of vestibular migraine and Benign Paroxysmal Positional Vertigo. Attack frequency, nystagmus duration, whether the nystagmus onset was motion provoked, nystagmus direction, slow phase velocity and slow phase duration were found to be discriminatory features that could be exploited to allow an automated diagnosis to be made.

Conclusions: The data provided by vestibular telemetry can be used to differentiate between different inner-ear causes of dizziness.

Introduction

Ménière's disease, vestibular migraine and Benign Paroxysmal Positional Vertigo are three of the most common causes of vertigo.[1] Ménière's disease and vestibular migraine are chronic conditions affecting the inner ear that can result in repeated and prolonged episodes of vertigo, while Benign Paroxysmal Positional Vertigo is characterised by short and frequent periods of motion-provoked vertigo.[2]

The diagnosis of Ménière's disease and vestibular migraine is contentious as there are few definitive and objective tests, and there is a significant overlap in the symptoms that patients report.[3] Tests that are currently available are usually performed while patients are asymptomatic. Clinicians rely on the self-reporting of vertigo by patients, however an individual's interpretation of their dizziness is highly subjective and the language used by patients is often ambiguous.[4] Furthermore, patients can wake to find themselves experiencing a vertigo attack, making it impossible for them to provide an accurate account of attack onset.[5] While relatively straightforward to diagnose Benign Paroxysmal Positional Vertigo using the Dix-Hallpike diagnostic manoeuvre, some patients can wait several years before Benign Paroxysmal Positional Vertigo is suspected by their clinician. Therefore, patients suffering from Ménière's disease, vestibular migraine and Benign Paroxysmal Positional Vertigo can face extended periods of uncertainty with debilitating symptoms prior to receiving a correct diagnosis and access to treatment.[6]

Recent advances in the field of vestibular telemetry have allowed the continuous ambulatory assessment of individuals with dizziness, vertigo and balance disturbance.[7–9] The Continuous Ambulatory Vestibular Assessment system includes a piece of wearable technology, plus the algorithms necessary to analyse the data it records. Detailed information regarding the system is available elsewhere,[8] but in essence, it allows the near-continuous monitoring of eye and head movements of individuals experiencing dizziness, for up to thirty days at a time. Parallels can be drawn between this device and the 24-hour ECG tape that is used to identify cardiac arrhythmias.[10] To suit the extended duration of wear, the device has been designed to be lightweight, ergonomic, and easy for patients to maintain. The device records the corneo-retinal potential generated by the eyes, in a similar way to the electronystagmography (ENG) technology used in clinical settings to record eye movements during balance testing.[11] In recent years, video technology has largely superseded ENG, but video is not suitable for an ambulatory monitor, as patients typically shut their

eyes during dizziness, video goggles are cumbersome to apply and technically inefficient, and there are privacy concerns surrounding 24-hour video capture.

We have recently completed a healthy volunteer trial in which seventeen healthy participants wore our device for up to thirty days.[7] The data gathered was used to evaluate the diagnostic accuracy, reliability, acceptability and safety of the device. Following this work, we are currently undertaking a clinical investigation to evaluate the system's capability to identify periods of nystagmus experienced by patients with Ménière's disease, vestibular migraine and Benign Paroxysmal Positional Vertigo. Using data from participants enrolled onto this trial, we have undertaken proof of concept work with the objective of identifying features of nystagmus that could be used to differentiate our three conditions of interest. In this article, which is a step towards our future aim of developing this system to provide an automated diagnosis for patients with vertigo, we present the results of this proof of concept work.

Materials and Methods

The data analysed here is from participants enrolled onto a clinical trial to investigate the diagnostic accuracy of the Continuous Ambulatory Vestibular Assessment (CAVA®) device. This trial has a recruitment target of thirty-five participants, and sixteen participants have been enrolled onto the study to date. This study forms part of a larger body of work funded by the UK Medical Research Council to develop an advanced prototype medical system for detecting vertigo, and was reviewed and approved by the London-Dulwich Research Ethics Committee (IRAS Number: 261099).

The device (Figure 1) records the corneo-retinal potential produced by the eyes, simultaneously capturing horizontal and vertical eye movements. Five press stud ECG electrodes are contained within single-use electrode mounts that connect to a reusable, electronic earpiece. Two electrodes near the temples capture horizontal eye movements, two above the left eye record vertical movements, and an electrode positioned under the right ear provides a reference voltage. Each channel of eye movement is sampled at 42.67 Hz. The device also records head motions in three-axes, sampled at a rate of 20 Hz.

Participants in the trial were expected to wear the device for thirty consecutive days, for up to 23 hours a day. An hour each day was allocated for washing and to replace the device's electrode pads. The participants whose data are presented here were recruited as part of the initial unblinded "training" phase of the investigation, in order to provide data to assist with the development of our computer algorithms. In the event of experiencing an attack of rotatory vertigo, participants were instructed to press an event marker button on the device and to keep a written record of the attack start time and duration. This data was used to assist the research team with locating the associated nystagmus data within the long-term data.

Based on preliminary work,[9] together with our understanding of the distinctive characteristics of nystagmus produced by Ménière's disease, vestibular migraine and Benign Paroxysmal Positional Vertigo, we extracted a range of parameters from the nystagmus data to quantify the differences between our three target conditions. These parameters were determined before we initiated the study and included candidate parameters of potentially high discriminatory value – see table 1. Nystagmus was identified from the data using our semi-automated nystagmus analysis software, which identifies candidate nystagmus beats and presents them for manual confirmation or rejection.[8] The software automatically quantifies the nystagmus direction, slow phase velocity and slow phase direction and the remaining parameters (i.e. attack frequency, nystagmus duration and whether onset was motion-provoked) are determined through a combination of manual interpretation of the software output and data from the participants' trial diaries.

Results

Upon returning their devices after thirty days, three of the sixteen participants enrolled reported experiencing attacks of rotary vertigo whilst wearing the device. The remaining thirteen participants either reported experiencing non-specific symptoms of imbalance (for which nystagmus was not present), or they did not experience vertigo during the trial. We quantified the characteristics of the nystagmus from the three participants who reported rotatory vertigo to determine whether there were any identifiable differences between the three examples (see table 2). All features examined provided a degree of discriminatory power, with the only overlap being an absence of motion-provoked vertigo for Ménière's disease and vestibular migraine, and the frequency of attacks for these conditions. There were differences between all three conditions in terms of nystagmus duration, nystagmus direction, the temporal characteristics of nystagmus direction, and the velocity and duration of the nystagmus slow phases.

Participant one was a 53-year-old lady with a fifteen-year history of left sided unilateral Ménière's disease. Please refer to our previous work for a detailed timeline of this participant's vertigo and

associated nystagmus.[9] For reference, the participant had recently reported discrete episodes of rotatory vertigo lasting for several hours. During the trial, the participant reported a single episode of vertigo lasting for approximately two hours (see figure 2). The attack comprised eight periods of nystagmus, each lasting between approximately 21 and 460 seconds. Over the course of the attack, the nystagmus direction alternated from right-beating to left-beating, back to right-beating, and finally to left-beating.

Participant two was a 36-year-old lady with a 22-year history of vestibular migraine. She reported distinct episodes of rotatory vertigo lasting for up to an hour. During the trial, she reported a single attack of rotatory vertigo lasting for approximately an hour (see figure 3). This nystagmus trace is markedly different to that of participant one, as the slow phase durations are longer, the slow phase velocities are lower, and the nystagmus is more intermittent. The longer-term characteristics of the vertigo were also different, as the nystagmus direction did not change throughout the attack, and the attack was much shorter overall.

Participant three was a 56-year-old lady with a three-year history of positional vertigo. She reported periods of rotatory vertigo lasting for a few seconds at a time, which were initiated by moving her head into certain positions. During the trial, she reported sixteen attacks of rotatory vertigo, lasting for around 10 seconds at a time. With the participant's consent, she also underwent diagnostic Dix-Hallpike manoeuvres at follow-up appointments during the trial, while also wearing the device (see figure 4). The concurrent accelerometer data showed that nystagmus onset was preceded by a significant movement of the head, occurring approximately 12 minutes and 8 seconds after device activation. This movement is consistent with a right-sided Dix-Hallpike manoeuvre, and corresponds to the participant moving from an upright to a supine position, with the affected ear facing downwards. The horizontal eye-movement trace for this participant is very different to the traces from patients one and two, as it shows no evidence of jerk nystagmus. By contrast, the vertical trace was relatively stationary until the onset of nystagmus, which occurred at about 12 minutes 20 seconds after device activation. At that time, an oscillatory eye-movement is visible. Interestingly, the nystagmus subsided briefly and then resumed more intensely about 7 seconds later. As the second wave of the nystagmus progressed, the signal first increased and then decreased in amplitude, before finally ending. The total duration of the nystagmus was about 20 seconds.

Discussion

Strengths of the study

In this article we have provided valuable proof-of-concept data showing that three of the most common inner-ear causes of vertigo can be discriminated based on a range of quantifiable characteristics of nystagmus. Furthermore, data from our system is capable of providing this discriminative information. The scope and detail of this data was only possible due to the long-term duration of data capture and because patients wore the device during their normal daily activities, rather than during a limited assessment in a clinical setting. This provides reassurance that further insights could be obtained from studying a larger cohort of patients and confirms proof-of-concept that an automated algorithmic approach to diagnosing the cause of dizziness is possible.

Synopsis of key findings

All of the nystagmus parameters we explored provided a high level of discrimination between the three diseases under investigation. Two parameters could be used to discriminate Benign Paroxysmal Positional Vertigo from Ménière's disease and vestibular migraine (Attack frequency and Motion-provoked onset). Four parameters provided sufficient information to differentiate all three conditions (nystagmus duration, nystagmus direction, slow phase velocity and slow phase duration). When presented with the findings from the device, participants expressed agreement with the results, which provided a more precise account than the trial diaries kept by the participants.

Clinical applicability of the study

We have confirmed that there are characteristics of nystagmus which differ between three of the most common inner-ear causes of dizziness. Just as we have previously applied machine-learning to detect pathological nystagmus,[12] and similar techniques have been applied to other areas of otolaryngology, such as oncology and neurotology,[13] the features identified here could be used to develop a system to automatically diagnose the cause of a patient's vertigo. The amount of data captured by our device during thirty-days makes manual analysis by a clinician infeasible. An automated approach to diagnosis, such as that proposed here, could be used to efficiently identify candidate nystagmus signals without the need for time-consuming manual inspection of all available data. As the long-term parameters of the vestibular disorders presented here have been hitherto unavailable, it is also likely that future data from the device could be used to support or improve existing diagnostic guidelines and to shed further insight into other conditions resulting in vertigo.

The COVID-19 pandemic has led to unprecedented financial pressures on world economies and has motivated the need to find financial savings across all areas of public health services. In 2013, the estimated annual cost of patients attending an emergency department due to dizziness or vertigo was greater than 4 billion US$.[14] Routine use of a system such as ours would reduce the number of hospital visits and the number of diagnostic tests required before patients receive treatment, reducing the costs incurred to diagnose patients with dizziness. A further benefit of telehealth techniques such as ours is in helping to reduce the transmission of viruses, such as COVID-19, which is likely to remain a pertinent issue in medicine for years to come.

The potential to automatically differentiate between Ménière's disease and vestibular migraine is a key advantage of our system, as these conditions have a significant degree of overlap in their presentation. There is benefit in correctly diagnosing these conditions to provide access to appropriate treatments and to avoid unnecessary interventions, as their treatments vary in terms of invasiveness and risk. Patients with Ménière's disease may be treated with invasive injections into the middle ear which, as well as being unpleasant for patients, carries risks of infection, damage to the tympanic membrane and in rare cases, hearing loss. Although a range of drugs are available for patients with vestibular migraine, these drugs are not without risk and the process of finding the right drug can be time consuming. Delaying the correct treatment also prolongs the suffering of patients.

It might be argued that using our system to diagnose Benign Paroxysmal Positional Vertigo is unnecessary, as patients are often able to identify the link between head movements and the onset of dizziness, and it can be easily identified in clinical settings using the Dix-Hallpike manoeuvre. But not all patients will make this association and symptoms of dizziness upon head movement could indicate space and motion discomfort, rather than Benign Paroxysmal Positional Vertigo. The Dix-Hallpike test itself does not provide perfect diagnostic sensitivity.[15] We have encountered patients who, following a positive Dix-Hallpike test, produced a negative result 24-hours later, and a positive result after that. Therefore, considering only a single Dix-Hallpike test in isolation could lead to an incorrect diagnosis being made. While preceding head movements are one discriminatory characteristic of positional vertigo, nystagmus duration provides a further level of discrimination. The atypical nystagmus signal presented here is also a useful discriminator. In summary, there is potential value in using our system to diagnose patients reporting persistent and unexplained vertigo, for which Benign Paroxysmal Positional Vertigo could be one possible cause.

Patients enrolled onto our study expressed an increased willingness to explore the boundaries of their dizziness whilst wearing the device. For example, one participant with suspected Ménière's disease had reduced their salt, caffeine and alcohol intake, following information they'd obtained through their own research. During the patient's trial, they cautiously restarted eating these items and found them to have no impact on their dizziness symptoms. Such stories are common among patients with Ménière's disease or vestibular migraine, as patients seek to identify triggers for their vertigo. It is often easy for patients to form faulty generalisations by confusing coincidence with causality, leading to lifestyle limiting changes that have little or no effect on their symptoms. Our system gives patients the confidence to retest their assumptions and to remove such self-imposed restrictions on daily life.

Comparisons with other studies

There have been a handful of previous attempts to develop devices similar to ours, but all have had a number of limitations compared to the approach adopted here. Previous approaches have been limited in terms of the continuous duration of data capture, either due to data storage or battery requirements.[16–18] Most approaches require patients to apply and activate a device at the onset of dizziness,[17,18] which is challenging for patients experiencing an attack and this approach would not record pre-attack data such as the prodrome we have previously identified in a patient with Ménière's disease.[9] Despite their limitations, these previous attempts to develop a portable vertigo monitor do provide confirmation of the clinical need for and interest in a device such as this. More importantly, one of these studies was able to capture nystagmus from patients with Ménière's disease and vestibular migraine, and their results support our finding that the slow phase velocity is a discriminative feature of Ménière's disease and vestibular migraine.[18] Studies have also observed the direction-changing characteristics of Ménière's disease, whereby nystagmus direction alternates between left and right-beating during an attack, with more time spent beating towards the affected ear.[18–20] Our study has confirmed this finding and found it to be a useful factor for differentiating Ménière's disease from vestibular migraine.

Limitations of the study and further work

One limitation of this study is the low incidence of symptomatic patients recruited, with three out of sixteen patients experiencing rotatory vertigo during their thirty-day trial. To address this, we intend

to confirm our findings by conducting a much larger investigation involving several hundreds of patients. Beyond that, we will determine if vestibular telemetry could be used to distinguish a range of other conditions resulting in dizziness, such as acoustic neuroma, vestibular neuritis and stroke. Another limitation is that here we have used a semi-automatic analysis of the patient data to manually determine the discriminative features of our target conditions. In future, we intend to develop computer algorithms to fully automatically diagnose patients from the data provided by the device. There are a range of machine learning techniques which could be applied to this task, including traditional approaches and also more contemporary methods such as deep neural networks. We suggest that there are broadly two approaches to address this problem: firstly, the eye-movement signals themselves may be sufficiently informative to be discriminated directly. Secondly, a multi-stage approach might be better, whereby algorithms start by detecting the presence of nystagmus, and then the diagnosis is based upon higher-level features such as those described here. We hope that by sharing our findings with the scientific and medical communities, we may inspire others to focus their attentions on the emerging field of vestibular telemetry.

Declaration of Interest Statement

There are no relevant competing interests to declare.

Data Availability Statement

The data presented here is available upon reasonable request.

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Figure 1: The device includes a reusable logging module and two electrode mounts, containing five ECG electrodes. Patients can press the event marker button on the device to log the date and time of an activity of interest (e.g. an episode of dizziness). Holding the button for four seconds initiates the device's status check feature, with an LED then providing a visual warning of a low battery, a poor electrode connection, or normal device operation.

Figure 2: A 30-second horizontal eye-movement trace from an acute attack of Ménière's Disease, as captured by the device. A computer analysis was applied to these traces to automatically detect the fast (red) and slow (green) phases of the nystagmus, and the results were manually confirmed by a scientist. The analysis confirmed the presence of nystagmus, which alternated in direction throughout the attack and which is left-beating in this extract.

Figure 3: A 30-second horizontal eye-movement trace from an attack of vestibular migraine, as captured by the device. A computer analysis was applied to these traces to automatically detect the fast (red) and slow (green) phases of the nystagmus. The analysis confirmed the presence of nystagmus, which is right-beating for the entire duration of this attack.

Figure 4: 30-second (a) horizontal and (b) vertical eye-movement traces and (c) concurrent accelerometer trace from an attack of Benign Paroxysmal Positional Vertigo, as captured by the device. The three vertical black lines in each trace show activations of the device's event marker prior to the manoeuvre, approximately 5 seconds after the onset of nystagmus, and after the nystagmus had subsided. The eye-movement signals were analysed by manual inspection, as the traces are different to the "jerk" nystagmus shown in figures 2 and 3. The signals show an oscillatory eye movement, occurring predominantly in the vertical channel.