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### **Main Article**

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## White matter lesions in magnetic resonance imaging of the brain in 56 patients with visual vertigo

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#### Abstract

**Background.** Visual vertigo is defined as a condition in which there is worsening or triggering of vestibular symptoms in certain visual environments. Previous studies have associated visual vertigo with an increased prevalence of underlying white matter lesions on brain imaging.

**Method.** This study evaluated the magnetic resonance imaging scans of the brain from a cohort of patients with visual vertigo, and compared the outcomes to an age- and gender-matched group of healthy volunteers.

**Results and conclusion.** White matter lesions were observed in 17.9 per cent of the patient group and in 16.3 per cent of the control group. The prevalence of white matter lesions in the patient group was not too different to that expected based on age.

#### Introduction

Spatial orientation and postural control in humans is maintained by the effective central integration of vestibular, proprioceptive, visual and auditory cues.<sup>1</sup> Visual vertigo, or visually induced dizziness, is a term introduced by Bronstein to describe symptoms of dizziness, disorientation and/or unsteadiness in situations involving intense visual motion (e.g. walking down supermarket aisles). It is thought that visual vertigo results from an over-reliance on visual cues for perception and postural control (i.e. visual dependence), and it can follow insults to the vestibular system or other diseases affecting balance.<sup>2</sup>

A recent study found that patients who experience visually provoked dizziness or visual vertigo often have an increased prevalence of underlying white matter lesions compared to age-matched healthy individuals.<sup>3</sup> These lesions are thought to interfere with subcortical areas that are responsible for feedback inhibition, leading to excessive vestibular responses following exposure to challenging visual stimuli.<sup>3</sup>

This study aimed to evaluate the magnetic resonance imaging (MRI) brain scans of a cohort of patients with visual vertigo in a tertiary centre, and to compare the outcomes with an age- and gender-matched group of healthy volunteers.

#### **Materials and methods**

#### **Ethical considerations**

Ethical approval was granted, by the Yorkshire and the Humber – South Yorkshire Research Ethics Committee (reference: 09/H1310/79), to collect and analyse MRI scans from the control group. Approval from an ethics committee was not required in this study for the patient group, as the data described are routinely collected and assessed for service evaluation. The data were anonymised to protect patients' confidentiality.

#### Participants

We included all patients referred to the visual vertigo clinic of a tertiary referral centre between July 2013 and February 2016. These patients were initially assessed by an ENT surgeon, who then referred them to the visual vertigo clinic when appropriate. An MRI scan of the brain was requested in cases where a central lesion could not be ruled out.

The Regional Academic Unit of Radiology was approached to obtain data from MRI brain scans for our control group. Age- and gender-matched cases were selected through a search of an already existing database of MRI brain scans of healthy volunteers without dizziness or other medical problems.

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TABLE I DIAGNOSES, DEMOGRAPHICS AND QUESTIONNAIRE RESULTS OF VISUAL VERTIGO COHORT

Diagnosis*	Number of patients	Gender	Age (mean (range); years)	Situational Characteristics Questionnaire score (mean (range))
Vestibular neuritis	19	15 females & 4 males	48.5 (25–75)	2.24 (0.58-3.12)
Vestibular migraine	4	4 females	40.3 (20–57)	2.12 (1.21–2.88)
BPPV	7	5 females & 2 males	46.7 (33–68)	2.44 (1.2–3.32)
Ménière's disease	4	2 females & 2 males	55.8 (41-64)	2.69 (1.83–3.53)
Presbystasis or multifactorial dizziness	7	7 females	71 (58–85)	1.97 (0.38–3.2)
Vestibular schwannoma	3	1 female & 2 males	56.3 (45–65)	1.71 (0.91–2.88)
Fibromyalgia	3	3 females	45.3 (29–59)	2.60 (2.16–2.82)
Other	9	4 females & 5 males	49.2 (39–66)	2.33 (0.57-3.11)

\*Other diagnoses or causes of visual vertigo included: head injury (n = 2), surgery (n = 1), multiple sclerosis (n = 1), superior canal dehiscence (n = 1), idiopathic sporadic ataxia (n = 1), cerebellar stroke (n = 1), Mal de Debarquement (n = 1) and symptomatic orthostatic hypotension (n = 1). BPPV= benign paroxysmal positional vertigo

#### Situational Characteristics Questionnaire

The Situational Characteristics Questionnaire<sup>4</sup> is a validated, symptom-based questionnaire that measures the frequency of visually induced dizziness episodes. It is used to identify patients who suffer from visual vertigo when exposed to environments with visual-vestibular conflict or rich visual information (e.g. walking down long supermarket aisles or looking at a scrolling computer screen). Every patient completed the Situational Characteristics Questionnaire to assess the severity of their symptoms.

The Situational Characteristics Questionnaire comprises 19 questions with answers varying from 'never' (score of 0) to 'always' (score of 4). The final score is obtained by dividing the sum of all responses by the number of questions answered. Therefore, the final score ranges between 0 and 4. Scores greater than 0.9 indicate pathology, with a score of 4 signifying the worst symptoms.

#### Magnetic resonance imaging

We reviewed the MRI brain scans of included patients to assess for white matter lesions or other pathologies. The MRI was performed with a 1.5 T GE HDx scanner (General Electric Healthcare, Milwaukee, Wisconsin, USA). The protocol included axial T2-weighted, sagittal and coronal T1-weighted, isotropic high-resolution T2-weighted (through the posterior fossa if acoustic neuroma was suspected), diffusion-weighted imaging, and axial fluid-attenuated inversion recovery ('FLAIR').

Subsequently, the Fazekas classification,<sup>5</sup> which is used for grading small vessel disease changes, was used by a neuroradiologist to grade the presence of white matter lesions, in a blind manner to minimise bias. Deep white matter hyperintensity was graded as follows: 0 = absence, 1 = punctate foci, 2 = beginning confluence of foci and 3 = large confluent area. The MRI brain scans of an age- and gender-matched control group were subsequently assessed using the Fazekas classification.

#### Analysis

Statistical analysis was performed using the SPSS software package (SPSS, Chicago, Illinois, USA). The chi-square test was used to compare the prevalence of white matter lesions between the two groups (normal *vs* abnormal scans and visual vertigo *vs* control group). Significance levels were set at p < 0.05. TABLE II FAZEKAS CLASSIFICATION OF WHITE MATTER LESIONS\*

	Healthy vo	Healthy volunteers		Visual vertigo patients	
Grade	п	Mean age	п	Mean age	
1	6	48.3 years	6	60.5 years	
2	1	72 years	2	63.5 years	
3	0	-	2	59 years	

\*In the magnetic resonance imaging brain scans of healthy volunteers and patients with visual vertigo.

#### **Results**

Fifty-six patients with visual vertigo who underwent MRI of the brain were identified and included in this study. This group included 41 females and 15 males, with a mean age of 51.4 years (age range, 20–85 years). The mean Situational Characteristics Questionnaire score was 2.26 (range, 0.38– 3.53). The patients' demographics, diagnoses and questionnaire results are shown in Table I.

The frequency of white matter lesions in the patient group (Fazekas classification scale of 1-3) was 17.9 per cent. Specifically, six patients had grade 1 (mean age, 60.5 years), two patients had grade 2 (mean age, 63.5 years) and two patients had grade 3 (mean age, 59 years) (Table II).

The control group comprised 43 individuals (86 per cent matching). There were 29 females and 14 males, with a mean age of 48.6 years (age range, 19–72 years). The incidence of white matter lesions in this group was 16.3 per cent. Specifically, six patients had grade 1 (mean age, 48.3 years) and one patient had grade 2 (72 years old) (Table II).

#### Discussion

Appropriate spatial orientation and postural control in humans is maintained by the effective central integration of vestibular, proprioceptive, visual and auditory cues.<sup>1,6</sup> Often, patients with a peripheral or central vestibular disorder may experience symptoms of dizziness, disorientation and light-headedness when exposed to visually challenging environments (e.g. supermarket aisles, crowded places, corridors with fluorescent lights, motorways). Although the term 'visual vertigo syndrome' was introduced to characterise these symptoms, patients rarely describe true vertigo, but rather a sense of disorientation.<sup>2</sup> As occasionally visual vertigo is described in the absence of any vestibular insults, it has been thought to be of psychogenic origin.<sup>7</sup>

Patients with visual vertigo rely heavily on information received from non-vestibular channels for postural and perceptual responses, and become visually dependent.<sup>2,8</sup> It is believed that in the presence of a visual–vestibular mismatch (e.g. secondary to vestibular dysfunction), there is bilateral deactivation of the parieto-insular vestibular cortex, which likely represents an innate attempt to protect visual perception of self-motion.<sup>9</sup> Visual over-reliance is thought to delay central vestibular compensation, especially in environments with conflicting visual–vestibular cues.<sup>2,10</sup> These patients also develop avoidance behaviour, generalised anxiety, social disability and agoraphobia, which lead to social isolation and further delays to vestibular compensation.<sup>11,12</sup>

#### Synopsis of new findings

In our study, we included patients with a clinical diagnosis of visual vertigo secondary to many different causes, including vestibular neuritis, vestibular migraine and Ménière's disease. The control group comprised healthy volunteers, matched in terms of age and gender. White matter lesions were observed in 17.9 per cent of our patient group and in 16.3 per cent of the age- and gender-matched control group.

#### Study strengths

We have collected data from an over-subscribed visual vertigo clinic, from over a 2.5-year period. The study was also informed by outcomes of brain MRI scans of gender- and agematched healthy individuals. The Fazekas classification was used by a neuroradiologist to grade the presence of white matter lesions in both groups, in a blind manner to minimise bias.

#### Comparison with other studies

In a recently published study, brain abnormalities, in the form of non-specific white matter lesions, were observed in the MRI scans of patients with visual vertigo in a significantly higher frequency than in dizzy patients without visual vertigo. It was suggested that these lesions could interfere with normal vestibular perception, feedback inhibition and plasticity of the cerebral cortex.<sup>3</sup> Diffusion-tensor MRI showed that cerebral cortex white matter microstructure was attenuated in individuals adapted to visual stimulation (ballet dancers), but not in controls, indicating that the cerebral cortex plays a central role in vestibular perception and plasticity.<sup>13</sup> The prevalence of white matter lesions in the community elderly population has been found to be between 50 and 98 per cent. David et al. investigated the presence of white matter lesions in 141 asymptomatic individuals with an average age of 63 years; the prevalence of white matter lesions was found to be 26.2 per cent. The authors concluded that white matter lesions are common in healthy individuals aged over 50 years.<sup>14</sup>

#### Clinical applicability of study

The key message of our study is that the prevalence of white matter lesions is not too different between patients with visual vertigo and age- and gender-matched healthy individuals. Therefore, clinicians need to be cautious when attributing visual vertigo symptoms to the presence of white matter lesions, which is a non-reversible condition. On the contrary, patients should be encouraged to engage with their local rehabilitation services, which have proved to be effective.<sup>15</sup>

#### Study limitations

This is an observational, retrospective study and thus lacks the robustness of prospective, powered studies. Although the demographics of the patient and control groups were fairly similar, they were not identical; hence, confounding factors might have affected the results. Additionally, the small sample size, particularly in the control group, is a limitation of this study.

#### Future work

More work is needed to assess any relationship between white matter lesions and visual vertigo. Larger, well-designed, casecontrolled, prospective studies should compare the prevalence of white matter lesions between matched individuals suffering from dizziness and visual vertigo, dizziness without visual vertigo and healthy individuals. It would be interesting to assess whether patients with certain underlying diagnoses develop visual vertigo more often than others, and whether there is any association with other medical conditions, such as migraine, hypertension or diabetes. Moreover, studies of younger populations would be advantageous, as there would be fewer confounding factors, such as brain changes, attributable to ageing.

- Visual vertigo is defined by the worsening or triggering of vestibular symptoms in certain visual environments
- Visual vertigo has been associated with increased prevalence of white matter lesions in brain imaging
- This study evaluated the magnetic resonance imaging brain scans of patients with visual vertigo
- The outcomes were compared to an age- and gender-matched group of healthy volunteers
- White matter lesions were observed in 17.9 per cent of patients and 16.3 per cent of controls
- The prevalence of white matter lesions in patients was not too different than expected based on age

#### Conclusion

The prevalence of white matter lesions in our patient group was not higher than expected based on the age of this group. Larger, prospective, controlled studies need to be undertaken in this field.

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Competing interests. None declared

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