Vestibular Stimulation in Humans by Static Magnetic Fields of A 3T MRI Scanner – A Pilot Study

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ABSTRACT

Background: The presence of vertigo and nystagmus in high magnetic field opens up the possibility of using such a stimulation for clinical purposes. OBJECTIVE: The aim of this study was to test the possibility of vestibular activation, expressed by nystagmus, using a custom clinical MRI scanner.

Methods: Twelve volunteers were included. The right eye gaze location was recorded during introduction of the subject to the 3T MRI scanner's bore and during a similar movement outside the MRI suite. From the raw data from eyetracker Arrington, deviation angles of gaze and angular velocities and another parameters of nystagmus were calculated.

Results: All subjects presented the changes in eye movements direction and strength during introduction to the scanner. In control conditions, obtained nystagmus was predominantly vertical- this domination disappeared in magnetic field. The results presented a significant inter-subject variability. Movement on the scanner's table resulted in a larger and faster change in the pupil's position in X and Y axes (P<0.02). Compared to standard conditions, magnetic field tended to stabilize the movement in Y axis (P<0.02). Statistical analysis showed that during 120 s of observation, the maximal nystagmus was noted in 52,2s; the minimal in 71,6s. Nystagmus did not disappear, its frequency was 0,45. The direction of nystagmus in MRI was predominantly horizontal.

Conclusions: Introduction of healthy individuals into an MRI scanner during custom clinical conditions results in a vestibular activation that is different from the same movement outside artificial magnetic field. However, the reaction presents a significant inter-subject variability.

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Introduction

Magnetic resonance imaging (MRI) became a common diagnostic tool in almost all medical specialties. It is increasingly used for research and clinical purposes due to its non-invasiveness, excellent depiction of soft tissues, and presentation of functional data (Ngen and Artemov, 2017; Noguchi, 2016; Serafin et al., 2012) It is a common observation that certain vertigo-like sensations are reported by some subjects during MRI examinations and professionals working at MRI suites (Schenck, 1992; Liu, 2003; Gowland, 2005; Heilmaier et al., 2011). Those sensations seem to be related to the static magnetic field strength (Heinrich, 2013).

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A number of mechanisms by which magnetic fields may induce vertigo via stimulation of the vestibular system have been considered (Glover *et al.*, 2007). One explained the sensations as an effect of the field strength increase during the introduction of the subject to the scanner's bore, which in fact presents a gradient magnetic field (Heilmaier *et al.*, 2011; Glover *et al.*, 2007; Theysohn *et al.*, 2008). However, recently Roberts *et al.* showed that static high magnetic field may induce vertigo without any movement, and that vestibular stimulation in MRI bore is static and directional and results from a Lorentz force (Roberts *et al.*, 2011). They excluded the theory of electromagnetic induction and magnetic susceptibility as a source of magnetic vestibular stimulation. They observed no changes in slow phase velocity of the induced nystagmus, despite performing experiments with different amounts of electromagnetic induction (Roberts *et al.*, 2011).

The strong magnetic field produces a Lorentz force that is perpendicular to the field lines and to the ionic flow direction in ionic canals of hair cells. This force seems to be strong enough to push on the semicircular canal cupula, leading to nystagmus. Antunes *et al.* using a simplified model of the inner ear were able to calculate the pressures on the cupula due to Lorentz forces originated by ionic currents in a static magnetic field of 7 T (Antunes *et al.*, 2012). The model of stimulation is similar to angular acceleration and caloric stimulation of the labyrinth, that was confirmed by a linear transfer function of slow-phase velocity incorporating a low-pass term and a high-pass adaptation term (Glover *et al.*, 2014). The relationship to angular acceleration was also modeled by Jareonsettasin *et al.* (2016).

There are limited diagnostic tools to assess function of the vestibular system, leading to ambiguity about the correct diagnosis and targeted therapy. The presence of vertigo and nystagmus in high magnetic fields opens up the possibility of using such a stimulation for clinical purposes. However, recent papers were based on either very high field strength MRI units (even 7T) or a specialized equipment to normalize the movement of the subject into the scanner's bore (Schenck, 1992; Heilmaier *et al.*, 2011; Theysohn *et al.*, 2008; Roberts *et al.*, 2011; Antunes *et al.*, 2012). The aim of this study was to test the possibility of vestibular activation, which was expressed by eye movements, using a custom clinical MRI scanner generally available in medical care.

Material and Methods

The study group included twelve healthy right-handed volunteers aged 24-45 (mean 35,4) who were familiar with MR environment (had underwent at least one MR scanning previously). Exclusion criteria were as follows: episodes of vertigo or another otoneurological symptoms (hypoacusis, tinnitus, balance disturbances) in anamnesis, claustrophobia and other clinical contraindications to MRI, refractive error larger than 0.5 D, middle ear pathologies in anamnesis, an acute infection of the upper respiratory tract.

The test condition (MRI) was a movement of the subject on the MRI scanners table as during routine scanning. A standard commercial 3 T GE Discovery MR750 (GEHC, Waukesha, USA) scanner was used with a table movement speed of 10 cm/s. During the experiments no scanning was performed, i.e. no switched gradient magnetic field was applied. Therefore, only static magnetic field (B) was interacting with the subjects' vestibular organ. Subjects were introduced into the scanner's bore in a supine position with the head in body axis, eyetracker was placed on the right eye (Photo 1).

The control condition (standard) was a movement of the subject outside the MRI suiteusing the same direction and speed. An in-house built system was used that was composed of a trolley, a winch with electronic rotation speed control, and a tunnel of the same size as scanners bore. All the subjects were exposed to MRI system first and the control experiment was performed on the following day.

During experiments, the right eye movement was recorded with a dedicated MRI-conditional infrared camera (Visual System, NordicNeuroLab, Bergen, Norway) using a frequency of 50 Hz. A black background was used in both spectacles to avoid fixation. Instead, the subject was asked to look ahead. Testing rooms were entirely dark during experiments.

The eye movement was analyzed using ViewPoint EyeTracker® (Arrington Research, Inc., Scottsdale, AZ, USA) software. The location of the pupil in X and Y axes is the software's own technique. The pupil in the left upper corner was described as 0.0, 0.0, a value of 0.5, 0.5 indicated a central position, and 1.0, 1.0 was for the right lower corner. Analysis included data after normalization with respect to the relevant axes after an automatic smoothing, parallax correction. The data from 0 to 120 s of the experiment were used.

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Before every trial autocalibration was made. For a very good calibration we used 16 points; usually 9 provides to standard calibration. As a good practice we also integrated slip-correction into our experiments. Subject was looking straight ahead, position of gaze was approximately two-third of way up the monitor vertically and centered horizontally. We also ensured successful eye image thresholding.

The raw data included the time of the measurement and the location of the pupil in X and Y axes. MS Excel spreadsheet was used to calculate the time for the change in the pupil's position from the last measurement (dt), the change of the location (amplitude) in both axes (dX, dY), and the partial speed (velocity) of the gaze movement (vX, vY). Moreover, individual Coefficient of Variation (CV) was calculated for each subject as a ratio of the standard deviation to the mean. Statistical analysis was performed using MedCalc v. 14 (MedCalc Software bvba, Ostend, Belgium). Normality of the data distribution was assessed with the d'Agostino-Pearson's test. Between-subject characteristics of nystagmus were analyzed using the Friedman's test to establish whether or not the within-group variance allows for a joint analysis of the static magnetic field's influence on the eye movement. Comparison of the individual averaged characteristics between the test conditions and the control conditions was made with the paired samples t-test. P-values < 0.05 were considered statistically significant.

To describe the parameters of nystagmus Statistical analysis of raw data from eyetracker Arrington was performed by means of *Gaze Data Explorer* program with *Gaze Data Analysis* library prepared by Jacek Matulewski and the students cooperating with him in C# language in the environment of Visual Studio 2013. For the purposes of the present paper, the model was created used for data analysis in experiments with evoked nystagmus with the task of purposed fixation on a point. The program requires .NET 4 platform in Windows 7 and newer systems.

From the raw data, deviation angles of gaze at straight ahead position and angular velocities of eye movement were calculated. Periods of slow phase were determined on the basis of velocity criterion with the threshold velocity value of 2 degrees / second. Next, the slow phases the duration of which was shorter than 0.1 second, were excluded. In the course of the slow phase, maximum velocity was determined, which is connected with local maximum of velocity. This prevents the selection of velocity from the beginning and end of the slow phase, which can be the beginning or end of the neighboring fast phase. Also the minimum velocity was determined. Mean velocity was calculated taking into account the condition that velocities are smaller than the maximum velocity, therefore, here as well the values from the beginning and end were excluded.

Results

All experiments were performed successfully, and no subject interrupted the experiment due to vertigo. For every participant 1250 data points were collected in three categories: the time from the last measurement, pupil's position in X axis, and pupil's position in Y axis.

In control conditions, when lying on the movable table with no influence of magnetic field, observed eye movements were predominantly vertical (according to the movement of the table). When introduction to the scanner the vertical movements became not prevailing- horizontal movements often occurred stronger. An example of the gaze position analysis is presented on Fig. 1.

The results presented a significant inter-subject variability (Table 1).

There were statistically significant differences in the eyeball behavior during the test conditions and the control conditions. In every subject in control condition, both velocity of the eye movements and amplitude (changes in the pupil's position) were larger in Y axes than in X axes. Under test condition (MRI), the parameters in Y axes stopped to predominate over parameters in X (horizontal) axes. Moreover, MRI condition contrary to control, was related to the larger amplitude and faster velocity of the pupil both in X and Y axes. It means that the magnetic field was able not only to change the direction of eye movement normally observed during linear kinetic stimulation, but also to induce its higher intensity: amplitude and velocity. Those relations are presented in Table 2 and Fig. 2.

The MRI magnetic field had no impact on the variability of the subjects' eye movement in X axis. However, it tended *to stabilize* the movement in Y axis (Table 3, Fig. 3).

The velocities of the slow phase of nystagmus under MRI condition over time were introduced in the fig. 4, 5 (Fig. 4, Fig. 5).

Table 1. Mean values of the pupil position change in two axes (ΔX, ΔY) and the movement velocity (vX, vY) in particular subjects, and Coefficients of Variation (CV) of the means. Values are given for the test conditions (MRI) and the control conditions (Standard).

Subject	MR				Standard			
	*d*X	*d*Y	*v*X [s⁻¹]	*v* Y [s⁻¹]	dX	dY	*v* X [s⁻¹]	*v* Y [s⁻¹]
1	0.0122	0.0131	0.7337	0.7876	0.0081	0.0112	0.4873	0.6690
2	0.0092	0.0170	0.5553	1.0247	0.0059	0.0086	0.3513	0.5193
3	0.0204	0.0145	1.2228	0.8680	0.0063	0.0096	0.3816	0.5867
4	0.0528	0.0128	3.1785	0.7702	0.0064	0.0099	0.3846	0.5936
5	0.0152	0.0162	0.9119	0.9730	0.0085	0.0120	0.5072	0.7172
6	0.0279	0.0175	1.6722	1.0524	0.0069	0.0111	0.4160	0.6678
7	0.0155	0.0173	0.9354	1.0471	0.0088	0.0125	0.5331	0.7577
8	0.0225	0.0174	1.3708	1.0549	0.0104	0.0145	0.6225	0.8713
9	0.0295	0.0206	1.7708	1.2314	0.0076	0.0100	0.4602	0.6065
10	0.0169	0.0173	1.0103	1.0347	0.0061	0.0096	0.3674	0.5787
11	0.0250	0.0204	1.5099	1.2301	0.0075	0.0126	0.4513	0.7596
12	0.0155	0.0173	0.9354	1.0471	0.0079	0.0139	0.4774	0.8375
CV	0.5279	0.1441	0.5278	0.1442	0.1751	0.1633	0.1744	0.1617

Table 2. Comparison of the pupil position change in two axes (dX, dY) and the movement velocity (vX, vY) between the test conditions (MRI) and the control conditions (Standard). Mean values are given with their 95% Confidence Intervals. P-values based on the t-test.

Parameter	MR	Standard	P-value
*d*X	0.0219 (0.0145-0.0292)	0.0075 (0.0067-0.0084)	0.0015
*d*Y	0.0168 (0.0153-0.0183)	0.0113 (0.0101-0.01257)	<0.0001
*v*X [s⁻¹]	1.3173 (0.8756-1.7590)	0.4533 (0.4031-0.5036)	0.0015
*v*Y [s⁻¹]	1.0101 (0.9176-1.1026)	0.6804 (0.6105-0.7503)	<0.0001

Table 3. Comparison of the Coefficients of Variations (CV) for the pupil position change in two axes (dX, dY) and the movement velocity (vX, vY) between the test conditions (MRI) and the control conditions (Standard). Mean values are given with their 95% Confidence Intervals. P-values based on the t-test.

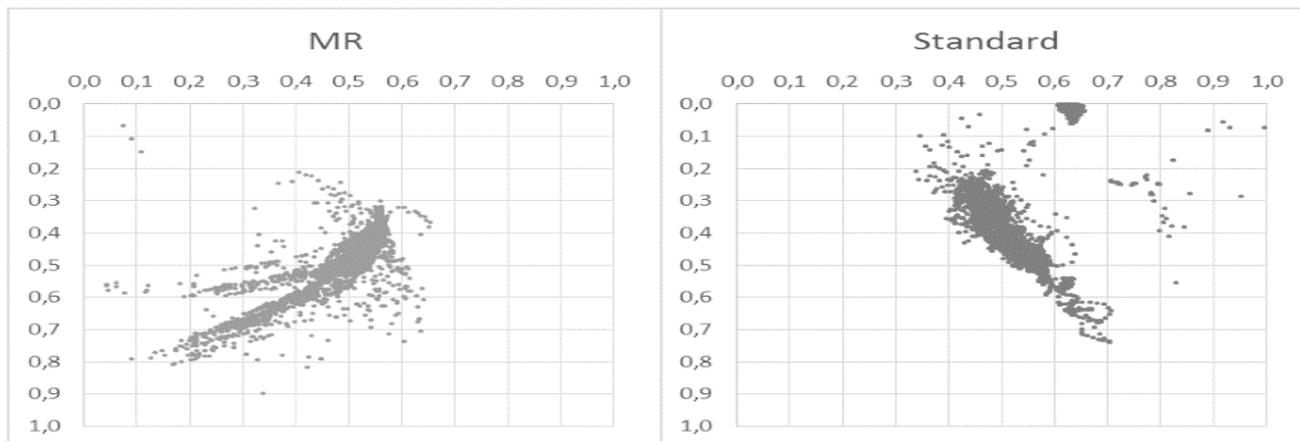| Parameter	MR	standard	p-value
CV$_{dX}$	2.41 (1.95-2.88)	2.17 (1.66-2.68)	0.5909
CV$_{dY}$	1.69 (1.55-1.84)	2.24 (1.92-2.56)	0.0109
CV$_{vX}$	2.42 (1.96-2.89)	2.19 (1.68-2.69)	0.5962
CV$_{vY}$	1.70 (1.56-1.84)	2.26 (1.94-2.58)	0.0097

Photo 1

Figure 1. Sample presentation of the pupil's position in subject No. 7 in the test conditions (MRI) and the control conditions (Standard). Numbers describe the gaze position in X and Y axes.
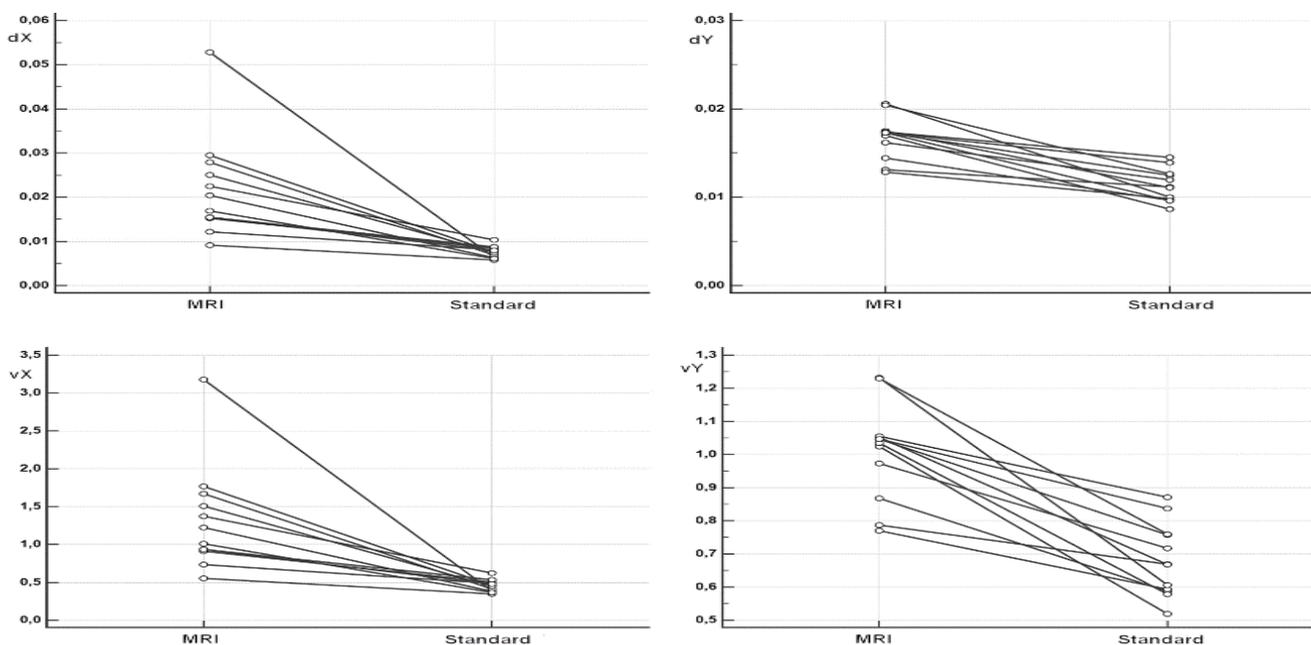

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Figure 2. Individual comparison of the change in the pupil's position (*d*X, *d*Y) and the velocity of its movement (*v*X, *v*Y). Points reflect subjects' mean values from the test conditions (MRI) and the control conditions (Standard).

Statistical analysis showed that during 120 s of observation, the maximal nystagmus was noted in 52,2s; the minimal in 71,6s. However, nystagmus did not disappear- it was still present during the whole time of observation, when magnetic field existed. The mean number of the nystagmus movements while 120 s was 55, so the frequency of nystagmus was 0,45. The direction of the nystagmus was properly reflected by the position of the pupil illustrated on the Fig. 1. The statistical analysis of Gaze Data Library from eyetracker Arrington revealed that under MRI the direction of nystagmus was predominantly horizontal; it could be precisely calculated on the base of the average number of 115,9 samples obtained to calculate parameters of slow phase velocity in one subject.

Discussion

In our pilot study we observed that a movement on a MRI scanner's table at custom clinical conditions results in a specific eye movements in healthy individuals, which may be considered as a vestibular activation. However, the eye movement parameters present a significant inter-subject variability that prohibits generalization.

A contemporary theory of magnetic vestibular stimulation resulting in vertigo and nystagmus seems to be established by Antunes *et al.* (Antunes *et al.*, 2012). Using a simplified spatial model of the inner ear, they calculated pressures on the cupula resulting from Lorentz forces originated by ionic currents in a
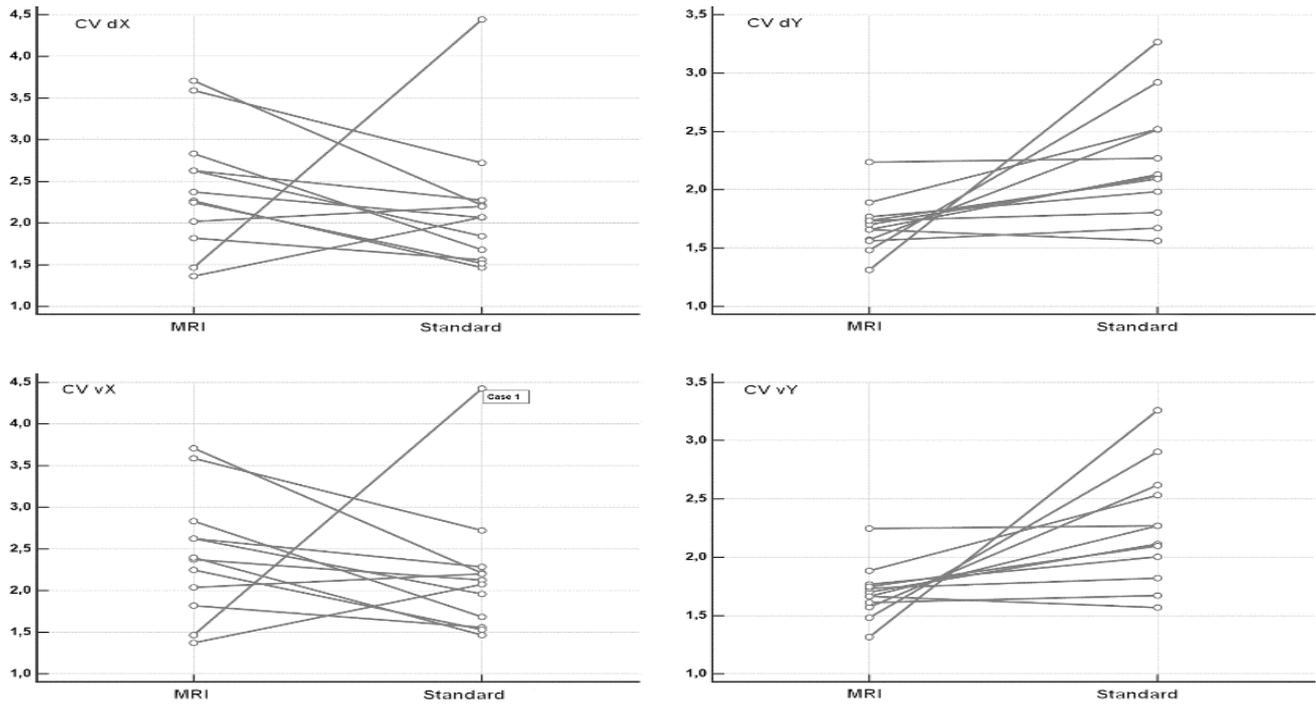
Figure 3. Individual comparison of the Coefficients of Variation (CV) for the change in the pupil's position (dX, dY) and the velocity of its movement (vX, vY). Points reflect subjects' values from the test conditions (MRI) and the control conditions (Standard).
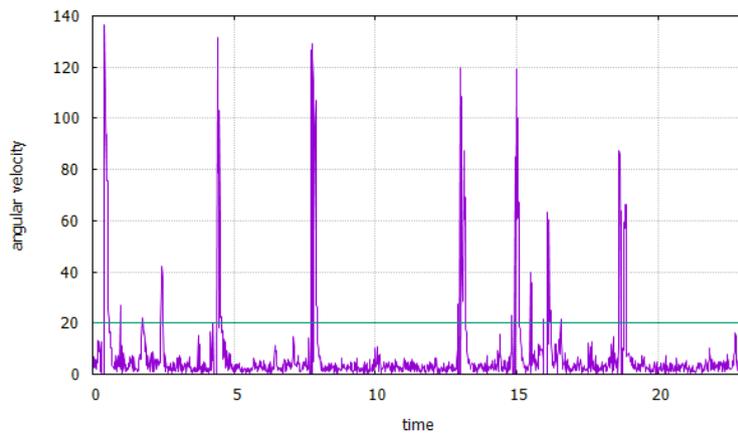
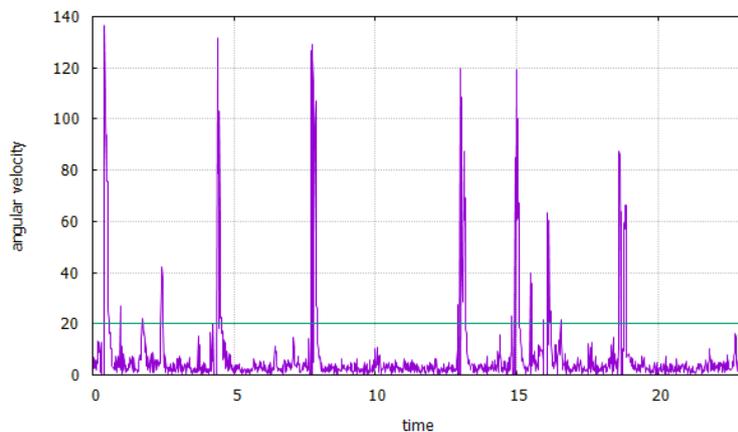**Figure 4.** The values of angular slow phase velocity [°/s] over time of MRI stimulation.a

Figure 5. The values of angular slow phase velocity [pixel/s] over time of MRI stimulation; linear velocity of the changes of pupil position on the virtual screen is proportional to angular velocity of small angles of deviations that occurs under tested condition.

static magnetic field of 7 T. Assuming for a hair-cell resting current of 100 pA per unit as well as field direction, geometry and localization of ionic sources and sinks as the dominant factors, they calculated that a maximum cupular pressure difference should be 1.6 mPa (Antunes *et al*., 2012). Roberts *et al*., (2011) suggested that Lorentz force is within the volume of endolymph fluid, not within the hair cells. In this model hair cells are pushed by pressing of cupula, not by direct electrical stimulation. The pressure needed for producing nystagmus is 0.1 mPa (Oman and Young, 1972).

It becomes clear in our study, that even lower than 7T magnetic static field like 3T is able to produce clinically sufficient eye movements. Moreover, such magnetic vestibular stimulation dominates over a kinetic one (table movement), changing the direction and strengthening the vestibular reaction. Acceleration and deceleration during bed movement into MRI bore, induced in lying position predominantly ampullas of posterior semicircular canals (apart from maculas) producing vertical eye movements, that were changed in direction and strength during influence of magnetic field.

Heinrich *et al*. studied the influence of 0 T, 1.5 T, 3 T, and 7 T MRI scanners on several subjective factors, including vertigo, in static and dynamic conditions (Heinrich *et al*., 2013). The maximum speed of movement in the dynamic mode was 9.2 cm/sec, which resulted in a maximum temporal change of magnetic field of 0.8 T/s. That study showed no significant difference in the sensation of vertigo between 7 T and other field strengths (Heinrich *et al*., 2013). Roberts *et al*. noted an increase in nystagmus velocity (objective sign) with static field strength, but with no reference to change in magnetic field gradient produced when subject moved on the table into the MRI bore (Roberts *et al*., 2011). Moreover, the nystagmus persisted even when the subject was laying inside the bore without any movement, like in our observations.

Mian *et al*. showed that the direction and magnitude of whole-body rotation sensation (vertigo) while stationary in a 7 T magnetic field was influenced by head orientation (Mian *et al*., 2016). The pitch angle changed the intensity of induced horizontal nystagmus; tilting head to the shoulder produced vertical nystagmus. In our study, the head position was controlled but small variation of the position during experiments could not be excluded.

This may partially explain the observed inter-subject variability of results. Generally under MRI condition, the intensity of eye movements in both axes (directions) significantly increased- were better expressed and moreover domination of vertical movements observed in control group disappeared. Roberts *et al*l. in similar conditions observed horizontal nystagmus- in laying position on the back, there are only corresponding semicircular canals of both ears that are responsible for stimulation of horizontal nystagmus (Roberts *et al*., 2011). In subjects with intact vestibular function on both sides, effects of magneto-hydrodynamic stimulation in the right and left lateral canal cupulae add up, and horizontal nystagmus is observed. The forces on the superior canal cupulae are inhibitory on the right and excitatory on left, so no vertical eye movements are observed. Otero-Millan *et al*. in 7T MRI also observed in healthy subjects horizontal pattern of nystagmus that was accompanied by torsional component (Otero-Millan *et al*., 2017).

Additionally, we observed that MRI decreased changes of parameters of eye movement in Y-axis. It might suggest that magnetic field induced not only peripheral vestibular structures but simultaneously affected central ones, including cerebellum (reputed to be responsible for stabilize vestibular function), finally resulting in less variation of vertical amplitude and velocity.

Clinical aspect of our study

Magnetic vestibular stimulation is an interesting phenomenon from a clinical point of view. A precise manipulation of the head position in the magnetic field may lead to a selective stimulation of different pairs of semicircular canals (Shaikh, 2012). Thus, the reason of clinical nystagmus may be linked to a particular semicircular canal. It will be useful for choosing the precise rehabilitation manoeuvre in patients with benign paroxysmal positional nystagmus (BPPV) originated from the particular semicircular canal. The changing of head position in such a way to put the particular semicircular canal in position perpendicular to the Lorentz force would lead to nystagmus originating directly from this induced canal.

Moreover, since the utricle- an important part of labyrinth engaged in linear acceleration and gravity detection appears to make an important contribution to the Lorenz force, the magnetic vestibular stimulation may be considered for a test

of the utricle function (Mian *et al.*, 2016). Till now, utricle function has become the most difficult to establish in clinical practice.

As the ionic composition of the endolymph and the number of hair cells in both the utricle and canals' ampullas are important determinants of the amplitude of the Lorentz force, magnetic stimulation can be used to monitor the effects of pharmacotherapy in labyrinth diseases. The limitation of such study is the geometric model of labyrinth and perpendicular relationship between Lorentz forces and ion current flow that excludes the simultaneous observation of both utricle and semicircular canals.

There are a lot of clinical situations when the unilateral vestibular function is observed (for example Meniere's disease). The standard procedure for its detection is caloric binaural test, not comfortable for the patient and rather long. With the use of MRI vertical and torsional nystagmus could be observed in unilateral vestibular hypofunction. MRI can help not only to find out the labyrinth hypofunction but to show which side is destroyed: In patients with left-sided loss, the force on the right superior canal cupula is inhibitory, and downward slow-phase nystagmus is noted in the magnetic field. In right labyrinth loss, the force on the left superior canal cupula is excitatory and magnetic stimulation develops upward nystagmus (Ward *et al.*, 2014).

Looking for the future, recent studies, including our report, may raise an idea to develop a system for clinical evaluation of vertigo. The system may include a movement in a static magnetic field or, preferably, a powerful magnetic field coil that would simulate our test conditions. Such a small coil would be much easier to use but it would require a precise calibration of the field strength. During the introduction to the scanner's bore, the subject was exposed to the field of increasing strength. However, only on the scanner's tunnel the field may be considered homogeneous. Outside the bore magnetic field lines are concentric and non-linear (van Nierop *et al.*, 2012). Furthermore, some local field inhomogenities related to the construction of the MRI suite and Faraday's cage may be of importance. Thus, a construction of a diagnostic tool for vertigo based on our observations has to consider several variables.

There are some limitations to our study that have to be addressed. Firstly, examinations included a small number of subjects. The size of the group was sufficient for a pilot study to prove the effect of the movement in static magnetic field on eye movements. However, a larger population should be included to explain the observed inter-subject variability and to find the threshold of the field strength that activated labyrinth. Secondly, although special attention was paid to the reproducibility of experiments' conditions, some potentially important parameters were not considered including the temperature, lighting, air movement due to air conditioning, and noise. Finally, some psychological factors that may influence eye movements, e.g. subclinical claustrophobia, were not analyzed.

Conclusions

Introduction of healthy individuals into an MRI scanner during custom clinical conditions results in a vestibular activation that is different from the same movement outside artificial magnetic field. However, the reaction presents a significant inter-subject variability. Further studies are necessary to test this phenomenon in patients suffering vertigo and to translate our observations into developing a clinical tool that would use magnetic field to diagnose such patients.

Because nowadays, MRI is the standard tool in diagnosis of the head, it may be additionally used for estimation of not only structure but function of the labyrinth as well.

Authors' Contribution

AW participated in the protocol development, data acquisition, and manuscript writing. KPO was involved in study design, funding application, recruiting the patients and manuscript writing. SO participated in study design and supervised the data acquisition. HK was involved in patient recruitment, data analysis and revising the manuscript. MM participated in data collection and analysis. ZS supervised the study, analyzed the data, and was involved in manuscript writing.

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