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Is activation of the vestibular system by electromagnetic induction a possibility in an MRI context?

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Abstract

In recent years, an increasing number of studies have discussed the mechanisms of vestibular activation in strong magnetic field settings such as occur in a magnetic resonance imaging scanner environment. Amid the different hypotheses, the Lorentz force explanation currently stands out as the most plausible mechanism, as evidenced by activation of the vestibulo-ocular reflex. Other hypotheses have largely been discarded. Nonetheless, both human data and computational modeling suggest that electromagnetic induction could be a valid mechanism which may coexist alongside the Lorentz force. To further investigate the induction hypothesis, we provide, herein, a first of its kind dosimetric analysis to estimate the induced electric fields at the vestibular system and compare them with what galvanic vestibular stimulation would generate. We found that electric field strengths from induction match galvanic vestibular stimulation strengths generating vestibular responses. This review examines the evidence in support of electromagnetic induction of vestibular responses, and whether movement-induced time-varying magnetic fields should be further considered and investigated.

KEYWORDS

dosimetry, electromagnetic induction, galvanic vestibular stimulation (GVS), Lorentz force, magnetic resonance imaging (MRI), vestibular system

1 | INTRODUCTION

Workers and patients moving in the vicinity of magnetic resonance imaging (MRI) scanners or directly lying inside the bore often report transient sensory sensations such as vertigo, dizziness, and nausea (Heilmaier et al., 2011; Heinrich et al., 2013; Rauschenberg et al., 2014), and illusions of rotating movements (Glover et al., 2007). Such perceptions suggest an interaction between magnetic fields (MF) and the vestibular system which have raised heightened safety concerns regarding potential risks and health effects associated with MRI use. Consequently, this has spurred investigations into the prevalence of signs and symptoms among individuals engaged in various MRI-related activities, encompassing those employed

in healthcare and research MRI facilities, as well as those contributing to the development of MRI systems. Indeed, during the last decade, the ongoing progress in MRI technologies has renewed attention to safety concerns for volunteers, patients, physicians, and service personnel. Therefore, despite administrations such as the American FDA (Food and Drug Administration) classifying MR systems up to 8 T as “without significant risk” for humans older than 1 month (Food and Drug Administration, 2003), it is still paramount to fully grasp the extent of the MFs effects on human neurophysiology to comprehensively guarantee the safety of the individuals engaged in such environment.,

Several reported hypotheses (Glover et al., 2007; Ward, Roberts, et al., 2015) have been proposed as potential modulatory mechanisms. However, to date,

only the Lorentz force mechanism is supported by experimental data (Roberts et al., 2011). According to the hypothesis, strong static MFs interact with the vestibular system via a continuous force acting on natural ionic currents within the vestibular system. This will be referred to as the “continuous Lorentz force mechanism” in this review. This evidence has pushed some authors to either reject or, at least, be less supportive of other hypotheses (Glover, 2015; Gowland & Glover, 2014; Ward, Roberts, et al., 2015). Yet, other researchers still argue that electromagnetic induction caused by body motion in a static MF, once the dominant hypothesis (Glover et al., 2007), is still a plausible mechanism (Laakso et al., 2013; Schaap et al., 2015). This review explores current knowledge to investigate whether activation of the vestibular system by electromagnetic induction within an MRI setting remains a reasonable hypothesis.

2 | THE VESTIBULAR SYSTEM: AN OVERVIEW

The vestibular system lies within the inner ear. Its main structure consists of a labyrinth of membranous tubules filled with endolymph fluid, which is contiguous with the auditory component of the inner ear (i.e., cochlea) (Figure 1a) (Baloh et al., 2011; Goldberg et al., 2012; Khan & Chang, 2013). Two distinct subsystems constitute the vestibular system: the semicircular canals (Figure 1b) and the otolith organs (Figure 1c). The former transduces rotational head motion. The latter, found within the utricle and saccule, detect horizontal and vertical linear accelerations of the head respectively, as well as the gravitational pull. This is done by transducing mechanical information

Highlights

- Vestibular system may be affected by motion-induced electric fields in magnetic resonance imaging (MRI) environment.
- Dosimetry demonstrates equivalent electric fields either with induction or with Galvanic Vestibular Stimulation (GVS).
- Stereotyped Lorentz force outcomes might be modulated with low-intensity GVS.
- The effects of the MRI magnetic field on the vestibular system may include two parallel mechanisms: the Lorentz force and induction.

(i.e., head movement & tilt) into electrical information integrated at the Central Nervous System (CNS) level. The sensing elements of the vestibular system, found in both subsystems, are hair cells. Head movements produce a deflection of the hair cells towards or away from the kinocilium, ultimately modulating the frequency of action potentials transmitted to the CNS via the primary vestibular afferent (Goldberg et al., 2012; Khan & Chang, 2013).

The vestibular system works as a push-pull mechanism. This means that, as the firing rate of one side increases, the firing rate of the other simultaneously decreases. The brain compares the difference between the firing rates on both sides and interprets this as head movement.

Once the peripheral vestibular afferent information reaches the vestibular nuclei within the brainstem, it passes through the following main ascending and descending neurological pathways: (1) the vestibulo-

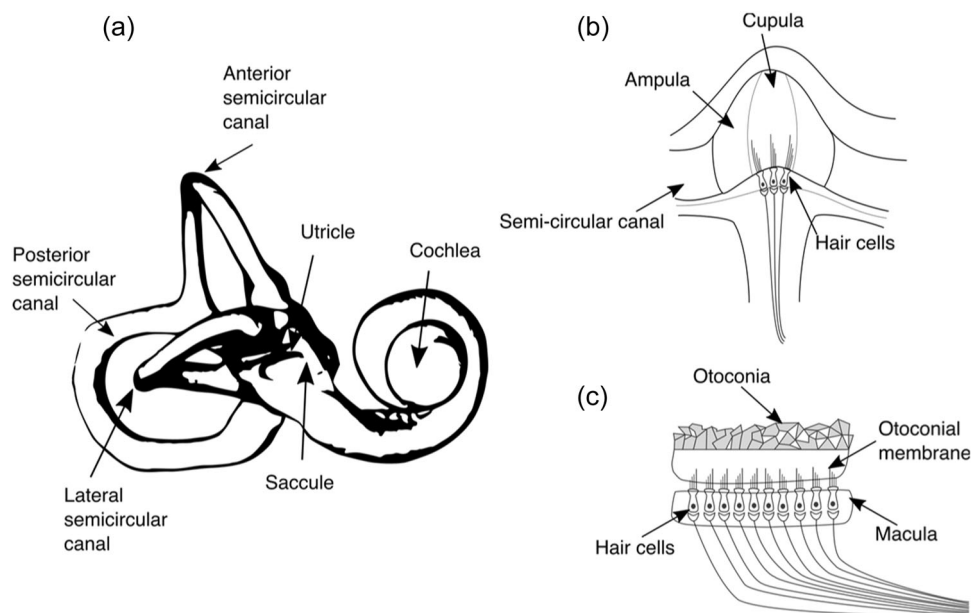


FIGURE 1 Overview of the vestibular system: (a) anatomical structures constituting the two vestibular subsystems. (b) The semicircular ducts end in the ampulla containing the hair cell receptors. A rotational acceleration of the head creates an endolymphatic flux displacing the cupula bending the cilia in the opposite direction of the rotation. (c) A linear acceleration or a static head tilt can displace the otolithic membrane creating shear forces bending the otolithic hair cells. Adapted from Purves et al. (2008).

ocular, (2) the vestibulospinal, (3) the vestibulo-thalamo-cortical, and (4) the vestibulo-autonomic pathways. Therefore, the vestibular system contributes to gaze stabilization, postural control and balance, cognitive functions such as perception of self-motion and spatial orientation (Cullen, 2019) as well as autonomic nervous system processes (Kerman et al., 2000; Yates et al., 2015; Yates & Bronstein, 2005; Yates & Miller, 1996).

3 | MFS AND THE VESTIBULAR SYSTEM: THEORETICAL MECHANISMS

Four physical mechanisms have been put forward to explain the impact of MF on the vestibular system (Ward et al., 2015): (1) the diamagnetic susceptibility (DS) of the vestibular system, (2) magneto-Hydro-Dynamic (MHD) mechanisms, (3) continuous Lorentz force on naturally occurring ionic currents, and (4) electromagnetic induction based on Faraday's law. It is worth noting that the latter three mechanisms are fundamentally due to the same physical force, that is, the Lorentz force, which is the magnetic force acting on moving charge carriers.

3.1 | The diamagnetic susceptibility (DS)

Unlike the vestibular cupula in which there are no crystalline structures, the otoconia located in the utricle and saccule end organs consist of calcium carbonate bio-crystals. This gives the otolithic sub-system diamagnetic properties. Thus, when a static participant is subjected to a strong MF gradient, an induced repulsive force, proportional to the gradient of the magnetic energy density ($\sim \nabla B^2$), could repel the otolithic membrane creating a shear force triggering the hair cells (Figure 1c). However, this mechanism necessitates two conditions: (i) high field strength in the order of 7 T (Glover et al., 2007) and (ii) an inhomogeneous MF which can only occur when there is a MF gradient, away from the homogenous field found at the center of the bore (Ward, Roberts, et al., 2015). It has been estimated that the forces could be of the order of the perception threshold at the entrance to a 7 T magnet bore (Glover et al., 2007). Yet, even in these specific conditions, the human data linking an MF vestibular specific trigger do not match the DS hypothesis so far (Antunes et al., 2012; Glover et al., 2007; Ward, Roberts, et al., 2015). Indeed, DS-induced results would theoretically not depend on the MF polarity, whereas the vestibular outcomes recorded so far do (Jareonsettasin et al., 2016; Otero-Millan et al., 2017; Roberts et al., 2011; Ward, Roberts, et al., 2014). Furthermore, as the force is proportional to the squared MF, it should be negligible in 3 and 1.5 T MRI environments. Therefore, the DS hypothesis has been dismissed to this day.

3.2 | Magneto-hydrodynamic (MHD) forces

MHD forces require a moving conducting fluid within high-strength MF environments (Kangarlu & Robitaille, 2000). The strong MF acts on the charge carriers in the fluid, producing forces that alter the flow of the fluid. In MRI settings, the MHD mechanism is known to affect the blood flow in the aorta, also producing voltage signals that alter the electrocardiogram (Martin et al., 2012). Applying this mechanism to the vestibular system necessitates both high-velocity endolymphatic flux (i.e., vigorous head movements) within a strong MF environment. The MHD forces, if strong enough, could then modulate the cupula's deflections generated by the head movements. The minimal pressure difference that can deflect the cupula and lead to vestibular responses is approximately 100 μ Pa (Glover et al., 2007; Oman & Young, 1972; Roberts et al., 2011). If this threshold is exceeded, the result would be a mismatch between the head movements and actual cupula deflection, possibly inducing dizziness or vertigo-like symptoms.

However, taking a flux density of 7 T and an angular velocity of 10 rad/s in their model, Glover et al. (2007) found a pressure of 5.5 μ Pa which is under the threshold of 100 μ Pa. Therefore, such MHD forces were deemed too low to trigger a vestibular response (Glover et al., 2007). Thus, this hypothesis was considered irrelevant for vestibular stimulation in an MRI setting.

3.3 | Continuous Lorentz force

Contrary to motion-induced MHD forces, no head movement or fluid flow are required to invoke a continuous Lorentz force since the movement comes from the microscopic motion of charge carriers in the naturally occurring ionic currents within the vestibular system. Indeed, the vestibular endolymph is an ion-rich fluid, with potassium and calcium currents constantly flowing into the hair cells. The utricle plays an important role in this mechanism for two reasons: (i) the higher ionic currents found there, compared the ones found at the cupular level and (ii) its location close to both the anterior and the lateral canals. Indeed, there is approximately 33,000 hair cells at the utricle level. This is 4.5 times more than the number of hair cells found within a canalithic ampullae. Therefore, this is where the highest current density is found. When interacting with a high strength static magnetic fields (SMF), these ionic currents at the utricle level produce a continuous Lorentz force generating a strong enough pressure (Antunes et al., 2012; Roberts et al., 2011) to deflect the cupulas of both lateral and anterior semicircular canals (Otero-Millan et al., 2017; Ward, Roberts, et al., 2014) (Figure 2). Indeed, within a 7 T magnet, the Lorentz force pressure ranges from 2000 to 20,000 μ Pa (Roberts et al., 2011), which is well above the threshold of 100 μ Pa (Glover et al., 2007; Oman & Young, 1972; Roberts et al., 2011). Moreover, the pressure being directly proportional to the MF strength,

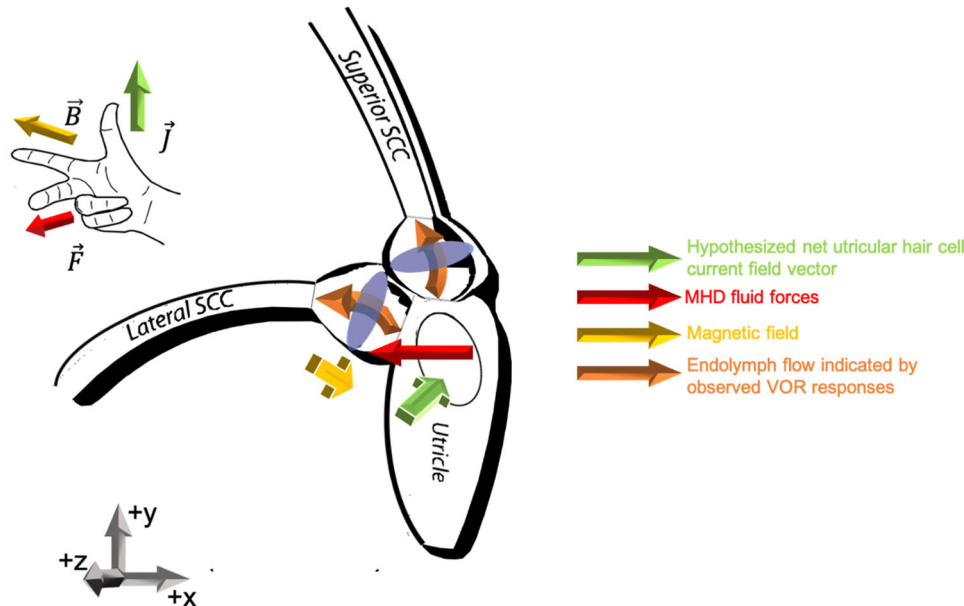


FIGURE 2 The continuous Lorentz force mechanism (Adapted from Ward et al., 2014): When interacting with a strong magnetic field (\vec{B} —yellow arrow), the utricular ionic current (\vec{J} —green arrow) results in a Lorentz force (\vec{F} —red arrow) inducing a sufficiently strong endolymph flow (orange arrows). Given the field's orientation, the Lorentz Force impacts predominantly the horizontal canal and to a lesser extent the superior canal. The right-hand rule shows the relationship between each vector. Axis represents the right, anterior, superior (RAS) radiological coordinate system [+X/right, +Y/anterior, +Z/superior].

the pressure can be estimated between 300 and 3000 μPa per 1 T. Thus, the pressure pushing on the cupulas would also be well above the 100 μPa threshold, even in a 1.5 T environment.

Due to the SMF orientation, the direction of the Lorentz force excites one ear while inhibiting the other (Ward, Roberts, et al., 2014). The asymmetry between the two sides mimics a constant head acceleration (Glover et al., 2014; Jareonsettasin et al., 2016; Shaikh, 2012), generating a clear nystagmus (Jareonsettasin et al., 2016; Otero-Millan et al., 2017; Roberts et al., 2011; Ward, Roberts, et al., 2014; Ward et al., 2015).

In a 7 T MRI bore, the horizontal component of recorded nystagmus peaks up to 40 deg/s before generally plateauing around a mean of 10 deg/s (Jareonsettasin et al., 2016). Furthermore, that response can last up to 90 min during the entire exposure, while participants lay still in the MRI bore (Jareonsettasin et al., 2016).

Up to date, backed up by mathematical modeling (Antunes et al., 2012) and both animal (Cason et al., 2009; Houpt et al., 2010, 2011, 2013; Houpt & Houpt, 2010; Ward, Tan, et al., 2014; Ward et al., 2018) and human (Otero-Millan et al., 2017; Roberts et al., 2011; Ward, Roberts, et al., 2014, 2015) experimental data, the continuous Lorentz force is the most thoroughly understood mechanism explaining the impact of high SMF on the vestibular system (Antunes et al., 2012; Jareonsettasin et al., 2016; Marcelli et al., 2009; Otero-Millan et al., 2017; Roberts et al., 2011; Ward, Roberts, et al., 2014; Ward et al., 2015).

3.4 | Electromagnetic induction

In an MRI setting, the strength of the MF proportionally decays with the distance from the bore, creating an

inhomogeneous SMF gradient. Therefore, moving through the inhomogeneous SMF gradient would expose the body to a changing flux density (B) over time.

Depending on the trajectory of the body through the SMF, the change in the MF can generate an eddy current and an electric field (E-field) in the body. The E-field generated by the motion in the SMF is equivalent to the E-field generated through electromagnetic induction in a stationary body that is exposed to a changing magnetic flux density (Bringuier, 2003). According to Faraday's law, a change in the MF flux density over time (dB/dt measured in T/s) will induce E-fields and currents within a conducting body. The higher the dB/dt , the higher the E-fields and currents. This is exemplified by the following equation that describes the induced E-field in a uniform conducting sphere: $E = \frac{r}{2} \frac{\partial B}{\partial t}$ [1], in which E is the E-field strength expressed in volts per meter (V/m) and r is the radius of the sphere in meters (m) within a homogeneous alternating flux density B .

Moving through the SMF's MRI gradient results in dB/dt and, according to equation (1), induced E-fields that not only depend on the SMF strength but also on the speed of movement. Depending on their strength, these fields can interfere with the human's own endogenous physiological electrical activity (Attwell, 2003; Hirata et al., 2011; Laakso & Hirata, 2012; Lövsund et al., 1979; Lövsund, Öberg, & Nilsson, 1980; Lövsund, Öberg, Nilsson, & Reuter, 1980).

Interestingly, the vestibular system is very sensitive to small E-fields and currents (Day et al., 2011; Długaczyc et al., 2019; Fitzpatrick & Day, 2004; Gensberger et al., 2016, 1984; Norris et al., 1998; Zenner et al., 1992). Indeed, applying electrical stimulation

between the mastoid processes, often known as Galvanic Vestibular Stimulation (GVS), triggers various vestibular outcomes (for reviews see Dlugaiczyk et al., 2019; Fitzpatrick & Day, 2004).

With electric stimulation, the intensity is more often reported in milliamperes (mA). However, estimation of the E-field strength in situ in the vestibular system is nontrivial, as it depends on the locations of the stimulation electrodes, anatomical features, and electrical conductivities of body tissues.

Thus, given that both GVS and electromagnetic induction produce E-fields, the latter has been hypothesized as a potential mechanism for activating the vestibular system (Glover et al., 2007). Nonetheless, compared to GVS, no clear dB/dt impact on the vestibular system has, to our knowledge, been recorded to date.

4 | REVISITING THE INDUCTION HYPOTHESIS

In the MRI setting, the recorded nystagmus responses are proportional to the SMF strength but are not correlated with the peak dB/dt induced when the participants are moved in and out of the MRI bore (Roberts et al., 2011; Ward, Roberts, et al., 2015). Furthermore, the recorded nystagmus lasts up to 90 min during the entire exposure, while participants lay still in the MRI bore (Jareonsettasin et al., 2016). This is largely in favor of the continuous Lorentz force mechanism and has pushed authors to drop the induction hypothesis as a potential vestibular triggering mechanism (Gowland & Glover, 2014; Ward et al., 2015).

However, inside the MRI bore, movements are, most of the time, induced by the bed going in and out of the MRI scanner. Unless bed speed is changed for research purposes (Glover et al., 2014; Roberts et al., 2011; Uwano et al., 2015), the speed inside the bore is standardized. Normal speed values are found around 0.10 m/s (Glover et al., 2014; Otero-Millan et al., 2017). With a 7 T MRI scanner, this speed impacts the dB/dt values. Ward, Roberts, et al. (2015) found peak dB/dt values that do not go higher than 0.75 T/s. Mian et al. (2013) found 0.69 T/s. Finally, Glover et al. (2007) found peak dB/dt values of 1 T/s in a 7 T MRI bore with a bed speed of 0.1 m/s. Altogether, with a 7 T MRI scanner, this gives average dB/dt values around 0.8 T/s. Modifying speed entry and exit from the bore, peak dB/dt values can reach 3.5 T/s (Roberts et al., 2011) but, to our knowledge, besides this exception, no dB/dt has been generated above that value within a 7 T MRI bore. Therefore, because of bed speed going in and out of a 7 T MRI core, peak dB/dt values found in research are, on average, around 0.8 T/s and peak values do not go above 3.5 T/s.

To account for a potential induction impact, we need to have an interpretative framework to help us evaluate the induced E-fields at on the vestibular system level. Yet, to the best of our knowledge, no specific dosimetry study has, until now, accurately

modeled the E-fields needed to trigger vestibular outcomes in an MRI setting.

Therefore, to be able to compare the vestibular outcomes triggered by currents used with GVS with the potential outcomes due to the induced E-fields and currents in an MRI setting, we propose, herein, to include a dosimetry work to give us the interpretative framework to help us move forward.

4.1 | Dosimetry of electric fields in the vestibular system

Ten anatomically realistic computational head models were used to estimate the current flow and E-field intensities in the inner ear. The models were created from T1- and T2-weighted magnetic resonance (MR) images of volunteers and segmented by tissue (Soldati & Laakso, 2020). Model for inner ear were segmented as a single structure composed of the vestibular system (i.e., the semicircular canals, utricle, saccule, and vestibule), cochlea and a part of the vestibulocochlear nerve. It was obtained using an in-house template model and thresholding the MR image intensities. Figure 3 visualizes the head and vestibular system models.

A discrete conductivity value was assigned for each tissue (Table 1). The conductivities, assumed to be homogeneous and isotropic, were sourced from literature data as in Nissi and Laakso (2022). The inner ear is composed of bony and membranous labyrinths that contain fluids with conductivities similar to cerebrospinal fluid (CSF; Parazzini et al., 2007). Therefore, the inner ear conductivity was set to that of a mixture of 50% CSF and 50% cancellous bone (0.314 S/m), calculated using the Maxwell Garnett formula.

E-field induced in the inner ear and vestibular system was examined for movement in a SMF and for GVS. For movement induced field, the model was placed in a homogeneous SMF with a given time-derivative of magnetic flux density (dB/dt). This was done to mimic the real induction situation, where dB/dt is due to translational and/or rotational motion in a nonuniform MF. The direction of the dB/dt was aligned with the “left-right” (X), “front-back” (Y), or “top-bottom” (Z) axis of the model. For GVS, direct current was applied through two circular electrodes (surface area 3 cm²) placed on the skin near the mastoid processes behind the ears. GVS current amplitude was set to 1 mA and dB/dt to 1 T/s.

E-field inside the models was approximated (Figure 3) by solving the electric scalar potential equation under quasi-static assumption and Neumann boundary conditions for a magnetic (Equation 1) or electric source (Equation 2):

$$\nabla \cdot \sigma \nabla \phi = -\nabla \cdot \sigma \frac{\partial \mathbf{A}}{\partial t}, \quad (1)$$

$$\nabla \cdot \sigma \nabla \phi = -\frac{\partial \rho_s}{\partial t}, \quad (2)$$

where σ is the electrical conductivity, ϕ is the scalar potential, \mathbf{A} is the magnetic vector potential and $\frac{\partial \rho_s}{\partial t}$ is

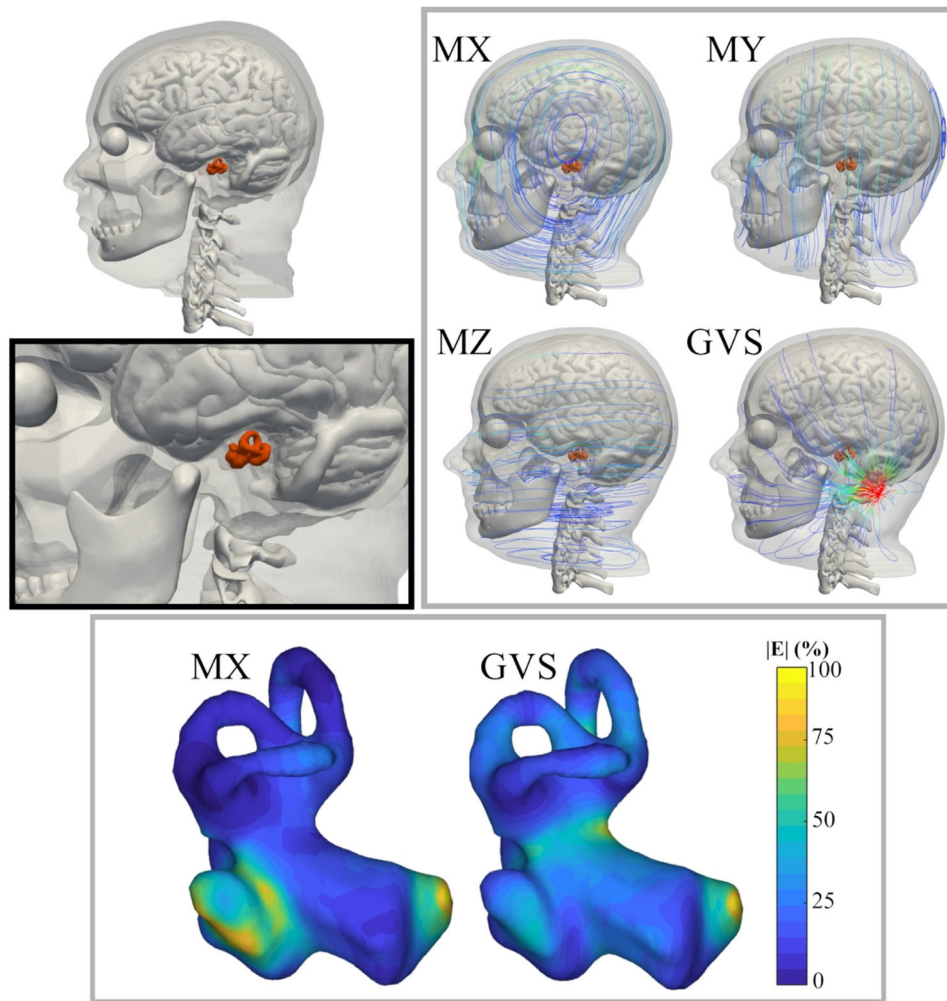


FIGURE 3 Dosimetry of E-field in the vestibular system: (Top-left) Tissue-segmented head model with structures of the inner ear highlighted. (Top-right) Streamline visualization of current flow induced by movement in magnetic field (dB/dt directions X , Y , and Z denoted with MX, MY, and MZ) or by galvanic vestibular stimulation (GVS). (Bottom) E-field strength in the inner ear (at 0.5 mm depth) for movement-induced field ($dB/dt = 1$ T/s) on the left and for GVS (1 mA) on the right.

TABLE 1 Electrical conductivities of biological tissues.

Tissue	S/m	Tissue	S/m
Blood	0.7	Fat	0.08
Bone (Cancellous)	0.027	Glands	0.5
Bone (Cortical)	0.008	Muscle	0.35
Brain (Gray matter)	0.2	Spinal cord	0.03
Brain (White matter)	0.14	Scalp	0.4
Cartilage	0.18	Tendon	0.3
Cerebellum	0.2	Trachea	0.3
Cerebrospinal fluid	1.8	Vitreous humor	1.55
Cornea	0.5	Retina	0.7

the source or sink of the electric current. The normal component of the current density was assumed to be zero on the model surface.

The head models were discretized into a uniform grid of cubical voxels with 0.5 mm resolution. This resulted in a system of linear equations was iteratively solved with an in-house algorithm based on the finite

element method (Laakso & Hirata, 2012) until the relative residual norm was less than 10^{-6} . The E-field inside each voxel of the target tissue was then calculated from the gradient of the scalar potential by

$$E = -\nabla\phi - \frac{\partial A}{\partial t}. \quad (3)$$

The mean intensity of the E-field within the vestibular system was first determined separately for each of the ten head models, then the group mean, and standard deviation were calculated across all models (Table 2). Superficial E-field at the 0.5 mm depth in the inner ear tissue was also calculated and visualized for one model with trilinear interpolation of the voxel data to a triangular surface (Figure 3, bottom panel).

As listed in Table 2, the direction of dB/dt had a minor effect on the mean E-field strength. Averaged over all directions, the induced E-field was approximately 12 mV/m per 1 T/s, which is used in the following to convert dB/dt to equivalent induced E-fields. For GVS, the current intensities are converted to equivalent E-field values by 38 mV/m per 1 mA. Therefore, the factor for converting dB/dt to equivalent GVS

TABLE 2 The mean and standard deviations of the E-field strength averaged over the inner ear for electromagnetic induction and galvanic vestibular stimulation (GVS).

Stimulus		Mean E (mV/m)
dB/dt (Y)	1 T/s	12.9 ± 3.0
dB/dt (Z)	1 T/s	11.6 ± 3.8
dB/dt (X)	1 T/s	10.9 ± 2.6
GVS	1 mA	38.3 ± 9.3

is 12/38 mA per T/s. We note that these conversion factors are order-of-magnitude estimates that do not account for differences for all experimental details, such as SMF inhomogeneity, movement trajectory, or the precise locations of the GVS electrodes.

4.2 | Estimated impact of the induced E-fields on the vestibular system

Based on our dosimetry work, 0.8 T/s translates on average to approximately 10 mV/m induced E-field strength (equivalent to GVS with 0.25 mA) and 3.5 T/s to 42 mV/m (again equivalent to GVS with 1.1 mA), which already produce ocular torsion responses (Severac Cauquil et al., 2003). According to Macdougall et al. (2003) such current intensities produce, in darkness, torsional nystagmus between 0.11 and 0.52 deg/s. This means that the induced currents in an MRI setting could be strong enough to generate very small nystagmus responses (Mackenzie & Reynolds, 2018; Severac Cauquil et al., 2003). Obviously this is a far lesser response than the peak horizontal 40 deg/sec nystagmus or the mean horizontal 10 deg/s plateau generated with the Lorentz Force seen in the MRI bore (Jareonsettasin et al., 2016; Otero-Millan et al., 2017). Indeed, 5 mA (190 mV/m) is needed to trigger a 2.5 deg/s nystagmus with GVS (Macdougall et al., 2003). Thus, it would take equivalent dB/dt of 16 T/s to produce only a nystagmus half as powerful as the one produced by the continuous Lorentz Force generated within a 7 T SMF when lying in the bore. Furthermore, such dB/dt levels can only be reached when participants vigorously shake their head within a 3 or 4 T bore (Glover et al., 2007). However, these head movements never occur in such experiments. Therefore, with the head still, in such settings, the stronger influence of the continuous Lorentz force should dwarf any potential vestibular stimulation generated by the weak induced currents.

5 | COULD GVS CONTRIBUTE TO OUR CURRENT UNDERSTANDING OF THE INDUCTION HYPOTHESIS?

Before the seminal work by Roberts et al. (2011), establishing the continuous Lorentz force as a vestibular-specific trigger, such a modulating mechanism was not taken into consideration during MRI

studies. While trying to understand the cortical activation due to vestibular stimulations, some authors used GVS during functional MRI (fMRI) recordings. Retrospectively, it is interesting to ponder if the GVS currents and the continuous Lorentz force potentially interact in an MRI setting.

The continuous Lorentz force is dependent on the magnitude of the SMF and its direction relative to the orientation to the vestibular system (Mian, Li, et al., 2015; Roberts et al., 2011). Therefore, it triggers particular outcome patterns in healthy subjects (Mian, Glover, et al., 2015; Roberts et al., 2011; Ward, Roberts, et al., 2015), which are modified in a very specific way depending on which semicircular canal is affected in patients (Ward, Roberts, et al., 2014). This generates stereotyped perceptions of movement. Healthy participants perceive they are moving around a naso-occipital axis as if the MRI bed spins around an earth-vertical axis (Mian, Glover, et al., 2015; Tarnutzer et al., 2023). Interestingly, the same roll perception around the naso-occipital axis applies when experimenters apply GVS to someone lying supine (Fitzpatrick et al., 2002).

When applied concurrently with rotation, GVS can either increase or oppose rotational perceptions depending on current polarity (Fitzpatrick et al., 2002). Because polarity changes with alternating-current GVS (AC-GVS), the perception of rotation switches direction. Within a 1.5 T MRI environment, Stephan et al. (2005) used a 2.5 mA AC-GVS (translating to approximately 95 mV/m) while their participants were lying still within the MRI bore. In that setting, most participants (63%) felt yaw rotation perceptions around the axis going through the head and feet and not the classical roll feeling. Also, in the same 1.5 T MRI environment, using GVS generating vestibular E-field strengths between 76 mV/m (2 mA) and 171 mV/m (4.5 mA) depending on individual perception thresholds, Bucher et al. (1998) also found interesting results. In this case, rotational perceptions were described around the nasal occipital axis in the roll plane. However, the directions were always dependent on GVS polarity. Indeed, the vestibular response was always oriented towards the anodal side and were therefore not correlated with the orientation of the MRI's SMF. Bense et al. (2001) confirmed the results of Bucher et al. (1998). In their experiment, the rotating perception once again switched from counterclockwise to clockwise with a change in GVS polarity.

These studies show that GVS stimulation within an MRI bore alters the stereotyped continuous Lorentz force response. Thus, sufficiently high induced current could do the same. Furthermore, these studies underline that E-fields strengths above 76 mV/m seem to alter or even counteract the continuous Lorentz force effects.

One could argue that 1.5 T could generate a sufficiently low continuous Lorentz force that could be countered by the GVS effects. However, Lobel et al. (1998) observed the same rotational perceptual effects in a 3 T MRI scanner with, on average, a 1.5 mA (57 mV/m) AC-GVS. Interestingly, inside the bore, the

perception was qualitatively similar as outside the bore but quantitatively less intense (Lobel et al., 1998). Given that the strength value of the SMF is higher at the center of the magnet's bore, this could be indicative of an interaction between the continuous Lorentz force and the GVS currents.

Stephan et al. (2005) distributed questionnaires to their participants exploring their self-motion perceptions in the bore while stimulated with AC-GVS. Interestingly, most of them did not report precise answers. There is a great inter-individual variability of intracranial E-field generated when electrodes are applied to the skull (Laakso et al., 2015). Our dosimetry results suggest that the E-field generated in the vestibular system by GVS is also variable between individuals, having coefficient of variation of 24% (Table 2). Therefore, for people more sensitive to GVS, conflicting information could arise between the continuous Lorentz force's stereotyped monodirectional spinning perception (Mian, Glover, et al., 2015) and the AC-GVS alternating rotational perception (Fitzpatrick et al., 2002), disorienting the participants in space.

Interestingly, 1 mA or 38 mV/m induces motion perception (Fitzpatrick et al., 2002; Lenggenhager et al., 2008). According to our dosimetry, 38 mV/m is induced on average by dB/dt of 3.2 T/s. To our knowledge, the highest dB/dt value found in the literature is 3.5 T/s, when Roberts et al. (2011) intentionally increased their bed speed in their experiment. This means, in this case, that strong enough time varying magnetic fields (TVMF) with higher dB/dt values could have had a perceptual effect. Yet no perceptual outcomes were analyzed in that study which only looked at eye movements induced via the vestibulo-ocular pathways (Roberts et al., 2011). Conversely, no eye movement recordings were obtained inside the MRI bore while researchers were stimulating

their participants with GVS (Bense et al., 2001; Bucher et al., 1998; Lobel et al., 1998; Stephan et al., 2005). Such recordings would have been fruitful as they would have enabled us to objectively see if electric currents impact the nystagmus generated by the continuous Lorentz force.

6 | IF INDUCTION THEORETICALLY TRIGGERS EYE MOVEMENTS IN MRI ENVIRONMENTS, THEN WHY HAVE THEY NOT BEEN RECORDED SO FAR?

The nystagmus response induced by the continuous Lorentz force can be inhibited by asking the participants to flex their neck at a certain angle varying from one person to another (Roberts et al., 2011). Indeed, this simple maneuver reorients the utricle in relation to the MRI's SMF. Interestingly, Roberts et al. (2011) did not record eye movements when the continuous Lorentz force was inhibited. This was taken as evidence that the eye movements were not coupled with the dB/dt peak value. However, at the time, the continuous Lorentz force was thought to only impact the horizontal canal (Roberts et al., 2011). Therefore, only horizontal eye movements were analyzed at 3.5 T/s (Roberts et al., 2011). Since then, Otero-Millan et al. (2017) confirmed that both the horizontal and the anterior canals were activated by the Lorentz force triggering three dimensional eye movements within the MRI bore. However, here again, no eye movement recordings were done when the continuous Lorentz force was inhibited by neck flexion. This is an important point to underline given that torsional eye movements are the primary outcomes with electric currents (Figure 4), especially when low intensities are used (Mackenzie

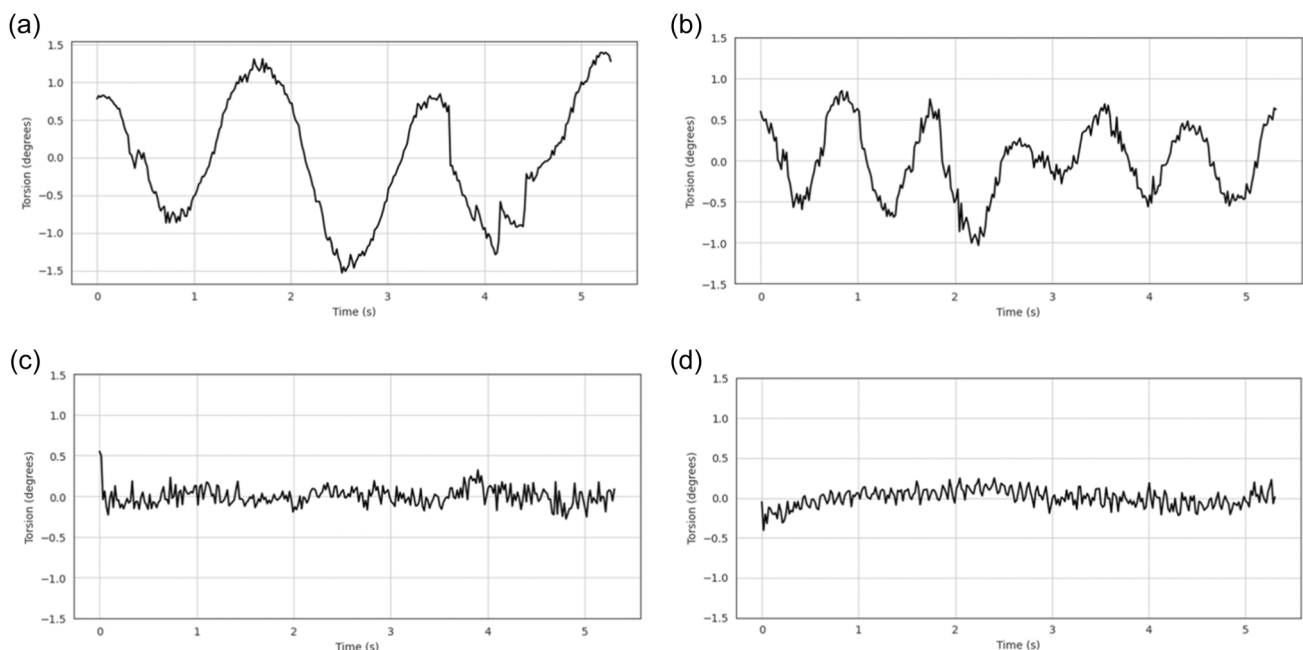


FIGURE 4 Characteristic torsional eye movements induced by ± 5 mA AC-GVS at 0.5 Hz (a), 1 Hz (b), 10 Hz (c), and 20 Hz (d).

et al., 2018; Schneider et al., 2000, 2002; Severac Cauquil et al., 2003; Watson et al., 1998; Zink et al., 1998). Thus, had the effect of the continuous Lorentz force been inhibited with neck flexion, and torsional eye movement analyzed, a more definitive answer could have been reached for the induction hypothesis. Yet, torsional eye movement amplitudes decrease significantly as the frequency of stimulation increases (Mackenzie & Reynolds, 2018) (Figure 4). This is relevant, as stimulation frequency depends on the speed of movement when one is pushed within the MRI bore. Small amplitude torsional eye movements analysis might need more sensitive image processing methods (Jin et al., 2020; Mackenzie & Reynolds, 2018; Otero-Millan et al., 2015). To further emphasize this specific point, we reanalyzed the data from Mackenzie and Reynolds (2018) using the method fully described in Otero-Millan et al. (2015) (Figure 4).

7 | MOVING FORWARD

Knowing whether induction is a potential mechanism in an MRI setting is an important issue for the overall safety of patients and workers alike. Within MRI vestibular literature, most authors now push forward the continuous Lorentz force hypothesis as the main mechanism triggering the vestibular system (Glover et al., 2014; Mian et al., 2013; Roberts et al., 2011; Ward, Roberts, et al., 2015). Yet, other authors still advocate for the induction as a valid mechanism (Laakso et al., 2013; Schaap et al., 2015). Thus, discarding the induction hypothesis could influence the international guidelines protecting both the public and the workers (Gowland & Glover, 2014).

After having their participants shake their head, Van Nierop et al. (2013) recorded postural adjustments in the vicinity of a 7 T MRI scanner. These results were obtained at 90 and 130 cm from the 7 T MRI bore where the flux densities were measured at 0.37 and at 0.24 T, respectively. Obviously, lower flux density would be measured in the vicinity of 1.5 and 3 T MRI scanners. Following a computational model, the continuous Lorentz force is thought to be strong enough to act on the cupula from 0.43 T (Antunes et al., 2012). Therefore, the question arises whether the postural control modulations found by Van Nierop et al. (2013) were indeed the results of the continuous Lorentz force. Considering flux density values lower than 0.43 T, we can only presume that, in these cases, the continuous Lorentz force would not be strong enough to trigger vestibular outcomes. Furthermore, these postural modulations were obtained with dB/dt values ranging up to 0.70 T/s on average, corresponding to 8.4 mV/m or 0.22 mA equivalent GVS, which could already trigger postural modulations for some people (Yang et al., 2015).

Furthermore, movements outside the bore are swifter and more complex than those inside the bore when lying on the bed. With normal daily movements, the physiological vestibular frequency range is thought

to be limited at 20 Hz (Goldberg et al., 2012). With more strenuous actions, this limit goes up to 30 Hz (Carriot et al., 2014). Therefore, in high Tesla environments, high dB/dt levels could likely be produced at the vestibular system level. This explains why moving outside the bore generates stronger dB/dt values than the ones obtained within the bore (Fuentes et al., 2008; Kännälä et al., 2009; De Vocht et al., 2012). Fuentes et al. (2008) have found peak dB/dt of 7.3 T/s obtained by normal body movements within a 1.5 MRI scanner environment. This corresponds to approximately 88 mV/m E-fields (2.3 mA equivalent GVS), which already induce rotational eye movements (Severac Cauquil et al., 2003) and destabilizes people, given that the postural control threshold can be found at levels as low as 8 mV/m (0.21 mA) (Yang et al., 2015). Moreover, in the same 1.5 T MRI scanner environment, where the flux density values were measured as being under 0.7 T, De Vocht et al. (2003) obtained dB/dt levels up to 50 T/s at head level. According to our dosimetry model, this translates to 16 mA equivalent GVS (600 mV/m) which would trigger strong vestibular outcomes. Therefore, in such 1.5 T MRI scanner conditions, where the continuous Lorentz force impact is low or even nonexistent (depending on the distance from the bore), the vestibular outcomes could be attributed to induction as pointed by our dosimetry work or a human study (Schaap et al., 2015). This seems all the more relevant with the 9.4 T MRI scanners used for brain imaging or research purposes (Cosmus & Parizh, 2011; Patel et al., 2008; Vaughan et al., 2006), not to mention the stronger 11.7 T MRIs (Quettier et al., 2017, 2018; Vedrine et al., 2010) or the predicted future 14–20 T MRIs (Budinger & Bird, 2018).

8 | CONCLUSION

We acknowledge the large impact of the continuous Lorentz force on the vestibular system. However, given the magnitude of the E-field theoretically induced within the vicinity of MRI scanners, it seems premature to completely exclude the induction hypothesis and its potential impact on the vestibular system. Thus, we feel more work is needed to confirm or dismiss the induction hypothesis. Two potential studies could be undertaken to investigate the induction hypothesis. The first could be to replicate the initial study done by Roberts et al. (2011). As was previously shown, the continuous Lorentz force impact could be inhibited by flexing the neck approximately around 30° accounting for inter-individual differences. The focus in this case would be to analyze whether torsional eye movements occur when peak dB/dt is induced. The second study of interest could be done outside the MRI environment to investigate the impact of TVMF vestibular specific stimulations on the vestibulo-ocular reflex pathway.

This could help close the debate on induction and would greatly enable the international agencies to provide better protection guidelines for both patients and workers within the MRI vicinity.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

ETHICS STATEMENT

This research was conducted in strict adherence to ethical principles and guidelines. Aalto University Research Ethics Committee, decision no. D/574/03.04/2022.

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