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Quantitative analysis of benign paroxysmal positional vertigo fatigue under canalithiasis conditions

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ABSTRACT

In our daily life, small flows in the semicircular canals (SCCs) of the inner ear displace a sensory structure called the cupula which mediates the transduction of head angular velocities to afferent signals. We consider a dysfunction of the SCCs known as canalithiasis. Under this condition, small debris particles disturb the flow in the SCCs and can cause benign paroxysmal positional vertigo (BPPV), arguably the most common form of vertigo in humans. The diagnosis of BPPV is mainly based on the analysis of typical eye movements (positional nystagmus) following provocative head maneuvers that are known to lead to vertigo in BPPV patients. These eye movements are triggered by the vestibulo-ocular reflex, and their velocity provides an indirect measurement of the cupula displacement. An attenuation of the vertigo and the nystagmus is often observed when the provocative maneuver is repeated. This attenuation is known as BPPV fatigue. It was not quantitatively described so far, and the mechanisms causing it remain unknown. We quantify fatigue by eye velocity measurements and propose a fluid dynamic interpretation of our results based on a computational model for the fluid–particle dynamics of a SCC with canalithiasis. Our model suggests that the particles may not go back to their initial position after a first head maneuver such that a second head maneuver leads to different particle trajectories causing smaller cupula displacements.

1. Introduction

The semicircular canals (SCCs) of the inner ear are the primary human sensors for head rotation. The SCCs are three, approximately mutually orthogonal, slender ducts which span an angle of approximately 250° and merge into a bigger chamber called utricle (Fig. 1). One end of each SCC has a larger cross-section, the ampulla, that is plugged by a gelatinous flexible structure, the cupula. The fluid which fills the SCC, the endolymph, lags the moving canal walls during head rotation such that it deflects the cupula and the embedded hair cell bundles. This displacement and the resulting afferent signals are proportional to the head velocity, and trigger compensatory eye movements [the Vestibulo-Ocular Reflex (VOR)], which rotate the eyes opposite to the head rotation, stabilizing the eye in space and reducing visual blur. If the eye moves too far from a central position, a fast corrective movement (saccade) returns the eyes to their central position. During prolonged stimulation, the alternating slow compensatory and fast resetting movements are called nystagmus.

A mechanical dysfunction of the SCCs, mainly of the posterior canal (PC), can lead to Benign Paroxysmal Positional Vertigo (BPPV), arguably the most common form of vertigo in humans (Baloh et al., 1989). This dysfunction is often associated with canalithiasis, a condition where free-floating particles (canaliths) reside in the SCC. Provocative head maneuvers (HM), e.g. when tilting the head backward to take a book from the top shelf, lift the particles to a higher position from which they can then settle under the action of gravity. This can lead to a flow similar to that induced by head rotations (Hall et al., 1979; Epley, 2001). The resulting post-rotatory cupula displacement triggers the misleading spinning sensation which is experienced during BPPV. The vertigo following the HM is revealed by a 'positional' nystagmus. This understanding of BPPV is supported by the intra-operative observation of particles in the membranous PC (Parnes and McClure, 1992), by several in-vivo models based on ampullary-afferents measurements (Suzuki et al., 1996; Inagaki et al., 2006; Rajguru and Rabbitt, 2007; Valli et al., 2009), and by several theoretical (House and Honrubia, 2003; Squires et al., 2004; Rajguru et al., 2004; Obrist and Hegemann, 2008; Boselli, 2012)

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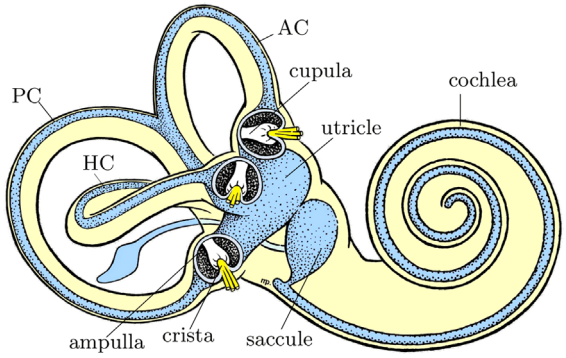

Fig. 1. The membranous labyrinth (blue) and the bony labyrinth (yellow) of the inner ear (adapted from Obrist et al., 2010). The width of the membranous anterior (AC), posterior (PC), and horizontal (HC) canals is exaggerated for better visibility. In reality their width is only about 5% of the diameter of the bony canals (Curthoys et al., 1977). (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this paper.)

and in vitro (Obrist et al., 2010) models. In the case where the particles stick to the cupula rather than float in the SCC, it is common to talk about "cupulolithiasis" rather than canalithiasis. Cupulolithiasis and canalithiasis can coexist and lead to a very similar nystagmus (Cohen and Sangi-Haghpeykar, 2010).

It is typical for BPPV that the positional nystagmus is generally weaker when the HM is repeated (Dix and Hallpike, 1952). This intricate phenomenon, known as BPPV *fatigue*, is usually attributed to the disintegration of particle lumps into smaller parts (Parnes and McClure, 1992; Parnes and Price-Jones, 1993; Parnes et al., 2003). However, previous theoretical studies do not support this mechanical interpretation of BPPV fatigue. Squires et al. (2004) concluded that a train of particles settling in a SCC would lead to a higher cupula displacement than a single particle of equal mass. Similarly, Rajguru and Rabbitt (2007) and Obrist and Hegemann (2008) repeated simulations of a HM by increasing the number of particles while keeping the total mass constant. This resulted in an increased cupula displacement rather than in 'fatigue'. These theoretical models, however, are based on the Stokes drag force of isolated spheres and cannot account for the interaction between particles. In contrast, Boselli (2012) introduced a model based on the force coupling method (Lomholt et al., 2002) which can account for the finite size of the particles and their hydrodynamic interaction. This model was able to predict up to a 40% reduction (i.e. a fatigue) of the cupula displacement but only if the particle lump before the first HM blocks almost the whole canal lumen. For this particle size, however, the particle-driven flow is dominant already during the HM, which is in contrast to typical nystagmus measurements where the particle-driven flow dominates only after the HM. Furthermore, these numerical experiments assume the resting particle position before the first and the second HM to be about the same. In the present work, we quantify the fatigue of the nystagmus in several patients and apply the model of Boselli (2012) to provide an interpretation of our nystagmus measurements based on the redistribution of particles in the SCC due to a HM.

2. Materials and methods

2.1. Nystagmus measurements

The fatigue of the positional BPPV nystagmus is discussed only qualitatively in the literature. Therefore, we started by analyzing clinical nystagmus measurements of nine patients and discuss how the nystagmus changes for repeated HMs. The experimental protocol was approved by the Ethics Committee of the Canton of Zurich, Switzerland, and all patients provided written consent after the experimental procedure was explained.

Patients sat in a motorized chair that rotated the subject about an axis that intersected the head orthogonally to the plane of the posterior canal. In a first head maneuver (HM1), the rotation was backwards by 120°. The rotation was done with a constant acceleration of 10°/s^2 for half of the movement (60°) and then decelerated with $-10°/s^2$ for the second half of the movement. This yields a triangular velocity profile with a peak of about 35°/s and a total duration of about 7 s (Fig. 2). The HM1 was then reversed, and the patient brought back upright. A second head maneuver (HM2), identical to HM1, was then applied in order to assess the fatigue of the nystagmus. Before applying any rotation, we waited until the patient's nystagmus and feelings of dizziness stopped (typically at least 60 s). The orientation of the SCC before and after these rotations is illustrated in Fig. 4. For two patients, a third HM was also applied after reversing HM2. Three-dimensional eye movements were measured by the scleral search coil technique (Collewijn et al., 1985), and the rotational velocity in the plane of the affected canal was calculated. The nystagmus was measured only during and after the backward rotations.

A reference light at gaze straight ahead was turned on at the start of the head rotation, and was turned off at the end. While this light suppressed eye movements during the head movement, distinguishing BPPV related nystagmus from the actual VOR would be difficult in any case.

Saccades were removed with an interactive computer program that automatically detected saccades when velocity exceeded a threshold (typically about 20°/s, depending upon the noise) above the median eye velocity calculated over a one second window. The automatically marked saccades could be manually adjusted and blink artifacts removed. The median velocity of each slow phase was calculated (Bockisch et al., 2013, 2012), and the resulting velocity trace was smoothed with a locally weighted second degree polynomial (`smooth.m` with a 10 s span, Mathworks).

All patients were diagnosed with posterior canal BPPV on examination and a positive response to a Dix–Hallpike maneuver. The patients had no other neurologic or eye movement disorders. Five patients had BPPV of the left posterior canal, and four of the right posterior canal.

2.2. Numerical model

The endolymph flow is modeled by the quasi-steady Stokes equations

$$-\nabla p(\mathbf{x},t)+\mu\nabla^2\mathbf{u}(\mathbf{x},t)=\mathbf{f}_c+\mathbf{f}_\alpha+\mathbf{f}_p \tag{1a}$$

$$\nabla\cdot\mathbf{u}(\mathbf{x},t)=0 \tag{1b}$$

with no-slip boundary conditions at the wall; t is the time, $\mathbf{x}=(x_1,x_2,x_3)$ are the Cartesian coordinates of the rotating reference frame, p and $\mathbf{u}=(u_1,u_2,u_3)$ are the pressure and the velocity of the fluid, respectively. The inertial force $\mathbf{f}_\alpha(\mathbf{x},t)\approx\rho\ddot{\boldsymbol{\alpha}}\times\mathbf{x}$ arises from the angular acceleration $\ddot{\boldsymbol{\alpha}}$ of the SCC during the head rotation (e.g. Boselli et al., 2013b; Oman et al., 1987); the force $\mathbf{f}_c$ is the restoring force of the cupula on the fluid; and $\mathbf{f}_p$ represents the forces exchanged between the particle and the fluid phases.

Cupula model: The force $\mathbf{f}_c$ is modeled as in the previous works (e.g. Oman et al., 1987) by introducing a pressure difference $\Delta P_c(t)=KV_c(t)$ across the cupula which is proportional to the volume V_c displaced by the HM and/or the particles, where K is the stiffness of the cupula. The volumetric displacement $V_c(t)$ of the cupula

$$V_c(t)=\int_0^t\iint_{A_c}\mathbf{u}\cdot\mathbf{n}_c\,\mathrm{d}A\,\mathrm{d}t \tag{2}$$

is computed numerically by time integration of the flow rate at a cross-section A_c of the SCC, where $\mathbf{n}_c$ is the normal vector on the surface A_c (Boselli et al., 2013b).

Fictitious forces: We adopt the force coupling method (FCM) and model each particle as a finite-size monopole (Maxey and Patel, 2001) such that $\mathbf{f}_p$ becomes

$$\mathbf{f}_p(\mathbf{x},t)=\sum_{\xi=1}^{n_p}\mathbf{F}_\xi\Delta_M(\mathbf{x}-\mathbf{Y}_\xi(t)) \tag{3}$$

where $\mathbf{Y}_\xi$ is the center of the ξ-th particle and n_p is the number of particles. The monopole strength $\mathbf{F}_\xi$ is given by the sum of the volumetric forces acting on the particle and includes the gravity force, attraction/repulsive forces between the particles, and wall-particle lubrication forces (Dance and Maxey, 2003). The lubrication force, if included, is precomputed for a single particle to match asymptotic solutions (Boselli, 2012). The sliding velocity of the particle at the wall depends on the minimum distance (lubrication gap) that is imposed between the particle and the wall. The force $\mathbf{F}_\xi$ is distributed over the particle volume by the force envelope Δ_M

$$\Delta_M(\mathbf{x}-\mathbf{Y}_\xi)=(2\pi\sigma_M^2)^{-3/2}\exp\left[\frac{-(\mathbf{x}-\mathbf{Y}_\xi)^2}{2\sigma_M^2}\right], \tag{4}$$

with the length scale $\sigma_M=a_p/\sqrt{\pi}$ similar to the particle radius a_p. The fluid domain is extended over the particle volume and the velocity $\mathbf{v}_\xi$ of each particle is given by the weighted average of $\mathbf{u}$ at the particle location

$$\mathbf{v}_\xi(t)=\int_{\mathbb{R}^3}\mathbf{u}(\mathbf{x},t)\Delta_M(\mathbf{x}-\mathbf{Y}_\xi(t))\,\mathrm{d}^3\mathbf{x}. \tag{5}$$

Eqs. (1) and (5) are solved by coupling the multilayer method of fundamental solutions (Boselli et al., 2012) to the FCM as proposed by Boselli et al. (2013a). We