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An MRI-compatible caloric stimulation device for the investigation of human vestibular cortex

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HIGHLIGHTS

- We present a new closed-loop MR-compatible delivery system for caloric vestibular stimulation (CVS) during fMRI.
- Chilled and hot water are repeatedly circulated simultaneously to left and right ear canals for robust CVS.
- In-scanner eyetracking reveals the onset of caloric nystagmus within the stimulation period.
- Functional MRI on a sample of 13 participants reveals activations in parieto-insular vestibular cortex (PIVC) and related cortical areas.
- This CVS delivery system can be combined with optic flow motion stimuli to study multisensory interactions underlying self-motion perception.

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ABSTRACT

Background: Self-motion perception involves the integration of vestibular, visual, somatosensory and other sensory cues. The neural responses to caloric vestibular stimulation (CVS) in humans have been investigated with functional magnetic resonance imaging (fMRI).
New method: We developed an fMRI-compatible, bithermal caloric stimulation device for repeated CVS. Tempered water is pumped via a closed-loop tube-system to one or both ear canals. Water temperature transmits to the surface of the ear canal via a small glass-pod. For our purposes we used hot (47–49 °C), cold (5–7.5 °C), or warm for baseline (30–32.5 °C). The pods are integrated in the MRI ear protection and connected to water influx and efflux tubes. With our device we can apply multiple vestibular stimulation and baseline trials consecutively. Control measurements indicate that the applied temperatures are stable across trials. MRI-signal differences due to water flow and water temperature are restricted to the area surrounding the pod and are unlikely to intrude into brain tissue.
Results: Vestibular stimulation with our device elicits caloric nystagmus when no central fixation is presented. We validated our system by conducting a CVS experiment during fMRI-scanning. Participants indicated the presence or absence of a self-motion sensation. Periods of self motion yielded activation in the cortical vestibular network including putative human parieto-insular vestibular cortex (PIVC).
Comparison with existing methods: Our closed-loop device eliminates many problems associated with caloric stimulation during fMRI.
Conclusions: Our device allows researchers to explore neural responses to CVS and those evoked by combined sensory stimulation.

1. Introduction

The vestibular sense is a primary sensory system that provides us with information about our current position and acceleration in space. It closely interacts with the visual system for the perception of self motion that arises when we move through our surroundings (Britten, 2008; DeAngelis and Angelaki, 2012). The vestibular sensors lie in the inner ear next to the cochlea of the auditory system in a structure called the bony labyrinth. The vestibular part of the labyrinth contains two otoliths (utricle and saccule) for the sensation of linear acceleration and gravity and three semicircular canals filled with endolymph for detection of angular acceleration. Afferents of the vestibular nerve propagate the information to the vestibular nuclei in pons and medulla, to posterolateral thalamus,

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and finally to cortex. This projection is referred to as the vestibulo-thalamo-cortical pathway (see Dieterich and Brandt, 2008). Other vestibular pathways project to the cerebellum, to medulla and pons in the brainstem, and to the spinal cord.

In primates several cortical areas have been identified for vestibular processing (see DeAngelis and Angelaki, 2012; Guldin and Grüsser, 1998; Lopez and Blanke, 2011, for reviews). Parieto-insular vestibular cortex (PIVC; Chen et al., 2010; Grüsser et al., 1990; Guldin and Grüsser, 1998) is often considered a core unit of the cortical vestibular system (e.g. Dieterich and Brandt, 2008; Lopez and Blanke, 2011).

Studies in monkeys used inertial motion of a platform where the animal was seated in a Bárány chair or on a moving platform for vestibular stimulation (see Chen et al., 2010; DeAngelis and Angelaki, 2012). A similar technique was applied in humans for psychophysical vestibular testing (Probst et al., 1995) and during simultaneous electroencephalographic recordings (Loose et al., 1999). The possibility to move the participant is greatly restricted inside the scanner (besides illusionary induced self motion via visual motion cues, e.g. Cardin and Smith, 2010) and thus most studies involving positron emission tomography or functional magnetic resonance imaging (fMRI) used caloric, galvanic, or auditory vestibular stimulation (Lopez et al., 2012a). Of all three techniques caloric stimulation is the most frequently used approach (see Lopez et al., 2012a; zu Eulenburg et al., 2012). It also plays an important role in clinical vestibular function testing (Brandt and Strupp, 2005; Dieterich and Brandt, 2008).

Caloric vestibular stimulation (CVS) uses hot and/or cold temperatures of water or other media that are applied to the ear canal and induce circulatory movements of the endolymph primarily in the horizontal semicircular canal located closest to the ear canal (Wuyts et al., 2007). Previous imaging studies provided temperature stimulation by means of direct injection of tempered water (Deutschländer et al., 2002; Dieterich et al., 2003; Suzuki et al., 2001), tempered air (Naito et al., 2003), or cooled nitrogen gas (Fasold et al., 2002) into the ear canal. Increasing the temperature of the endolymph in the horizontal canal evokes current movement toward the ampulla, a dilatation of the canal that contains the sensory neurons, whereas cold has the opposite effect (Bárány, 1907). Endolymph flow toward the ampulla depolarizes the sensory cells in the horizontal semicircular canals, thereby increasing firing in the vestibular nerve. If the flow is directed away from the ampulla the sensors are hyperpolarized and vestibular nerve firing is diminished compared to the firing rate during resting (baseline).

An advantage of the caloric approach is the stimulation of a specific vestibular sensor that evokes percepts of self motion in distinguishable directions. In our fMRI-experiment about which we will report below participants described the induced sensation of self motion as rotation in the roll- or yaw-plane (see also Deutschländer et al., 2002; Dieterich et al., 2003; Fasold et al., 2002) and predominantly indicated self motion away from the side of cold stimulation. Drawbacks of CVS, especially with tempered water, are that circulating water can lead to artifactual changes in the MRI-signal (Lobel et al., 1998), the problem of collecting the used water while the participant is still inside the scanner (see Deutschländer et al., 2002; Dieterich et al., 2003; Suzuki et al., 2001), and delays associated with temperature transduction within the temporal bone (Barnes, 1995).

Galvanic stimulation applies electrical current to the left and right neck mastoid processes and excites the entire vestibular nerve. This approach provides strong vestibular stimulation and elicits sensations of self motion, however, since all vestibular afferents are activated, the sensation is not merely experienced as simple rotation of the head to the left or right in the roll-/yaw-planes, but is more complex (Smith et al., 2012; Stephan et al., 2005). Brief auditory sounds of high intensity can lead to stimulation primarily in the saccular otolith, however, so far only few studies applied this technique for vestibular stimulation during functional imaging (e.g. Schlindwein et al., 2008).

We aimed to construct a caloric stimulation device that is compatible with the MRI-scanner environment while overcoming some of the previously mentioned problems of this technique. Our device enables us to perform multiple, consecutive stimulations with the same or different temperatures in either one or both ears (bithermal caloric stimulation, Anderson, 1995). It is a closed-loop system that avoids problems associated with water collection inside the scanner (see Mast et al., 2006, for a similar approach in a behavioral experiment).

In the following we will report on technical details of this new caloric stimulation device. We found that MRI-signal differences due to water circulation and water temperature are restricted to the immediate vicinity of the stimulation pods in the outer ear. CVS with our system elicited nystagmus when no central target was presented. We also conducted a vestibular localizer in 13 participants during fMRI-scanning. In this experiment participants indicated the presence or absence of self-motion sensations to the left or right. Based on previous findings we expected to find activation in the cortical vestibular network including putative human PIVC during periods of perceived self motion and concurrent CVS with our device.

2. Methods

2.1. Vestibular stimulation device

Our vestibular stimulation device allows for bithermal caloric stimulation using hot and cold distilled water. The water remains inside a closed-loop system and does not enter the ear canal. Fig. 1a shows the scheme of the stimulation apparatus. Images of the actual device are shown in Figs. 1b–d and 2. The following equipment is required to build the system: three plastic barrels, two temperature sensors, two mini-pumps, eight plastic tubes, a switching device to stimulate left and right ears with different water temperatures, two rigid glass-pods (each connected to a water influx and efflux tube) that are integrated in the left and right side of the MRI ear protection, and a plastic relay plate with a belt that is worn by the participant. In the following we will discuss every piece of the device in more detail and explain the mode of operation for the entire system.

Two barrels that can hold 25 l each are used to store hot and cold water (see 1 in Fig. 1a and b). Electronic thermometers (Hanna Instruments US, Woonsocket RI, USA) were placed in each barrel. Water was heated to ~50 °C (hot) in the one barrel or cooled with crushed ice to ~0 °C (cold) in the other barrel before starting vestibular stimulation. We measured temperatures continuously with thermal sensors and kept temperatures at constant levels throughout each vestibular experiment. This was done by refilling the respective barrel with either hot water or crushed ice. The third barrel had a volume of 50 l and it collected all returning water (5 in Fig. 1a and b). Two mini-pumps (Barwig Wasserversorgung, Bad Karlshafen, Germany) achieving a pressure of 0.6 bar each were placed deep inside the hot- and cold-water barrels. They are connected to two plastic tubes (red and blue solid lines on the left in Fig. 1a, diameter: 11 mm) and transport the tempered water to the switching device (2 in Figs. 1a and b and 2a). The switching device was located on a table in the scanner control room (distance between barrels and switching device: 1.5 m).

The plastic switching device was designed to allow for unilateral or bilateral stimulation with hot, cold, or warm. Same or different temperatures can be applied to the left and right ear canals at the same time. The device (see Fig. 2a for details) is custom-built and