Balancing the Self

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Contents

Abstract

The vestibular system is composed of otolith organs and semi-circular canals that encode linear and angular accelerations, as well as the position of the head with respect to gravity. Thus, the detection of self-motion, the distinction between self- and object-motion, as well as gaze stabilisation and maintenance of postural stability are the core vestibular functions. Recent research shows that vestibular information interacts with higher-level cognitive processes, such as space perception, attention orienting, body schema and bodily self-consciousness. In order to contribute to these faculties, vestibular information is dynamically combined with visual, somatosensory and proprioceptive signals. In the present thesis we explore such multimodal interactions using a human centrifuge (rotating chair). In Part 1 we show that visual and vestibular cues are integrated in accordance with statistical optimality even when large directional conflicts are introduced between these modalities. Participants were significantly better in discriminating rotation magnitude when simultaneously presented with visual and vestibular cues, as compared to each modality independently, despite the fact that the axes of rotation implied by the two cues were different (Study 1). We also demonstrate that visuo-vestibular integration is present and optimal in patients with unilateral vestibular loss (Study 2). Part 2 of the present thesis examined vestibular-somatosensory interactions. We show that vestibular stimulation in the form of passive whole-body rotations increases tactile sensitivity at the fingertips, as compared to a no-rotation baseline (Study 3). We also demonstrate that the effect of vestibular stimulation on touch is not direct, but mediated by visual information about self-motion: visual and vestibular cues first combine, and only subsequently influence tactile sensitivity (Study 4). In Part 3 of this thesis, we explored how vestibular stimulation affects visual attention and awareness. We show that when acting as an exogenous cue, vestibular stimulation orients attention at short cue-to-target delays. When acting as an endogenous cue, vestibular stimulation strongly orients attention at all cue-to-target delays (Study 5). Vestibular stimulation also affects visual awareness. Using a continuous flash suppression paradigm to suppress an optic flow stimulus during passive whole-body rotations, we show that optic flow that is congruent (i.e. counterdirectional) with the direction of the vestibular rotation breaks suppression faster than incongruent optic flow (Study 6). In sum, our findings refine the existing knowledge on multisensory processing in general and vestibular interactions with other senses in particular. Our results are of relevance for the understanding of how visual, vestibular, proprioceptive and somatosensory information are combined by the brain in order to form a coherent representation of the self in space.

Key words: vestibular, multisensory, visuo-vestibular integration, unilateral vestibular loss, tactile sensitivity, visual attention, visual awareness

Résumé

Le système vestibulaire, composé d'organes otolithiques et de canaux semi-circulaires, encode les accélérations linéaires et angulaires, ainsi que la position de la tête par rapport à la gravité. La détection de notre propre mouvement, la distinction entre notre mouvement et le mouvement d'objets extérieurs, ainsi que la stabilisation du regard et la maintenance de la stabilité posturale sont les fonctions vestibulaires principales. Des études récentes montrent que l'information vestibulaire interagit avec des fonctions cognitives de haut niveau, comme la perception de l'espace, l'orientation de l'attention, le schéma corporel et la conscience corporelle de soi. Afin de contribuer à ces facultés, l'information vestibulaire est combinée avec des signaux visuels, somatosensoriels et proprioceptifs. Dans ce travail de doctorat, nous examinons de telles interactions multimodales à l'aide d'une centrifuge humaine (la chaise rotatoire). Dans la première partie, nous démontrons que les signaux visuels et vestibulaires sont intégrés d'une façon optimale (selon les statistiques Bayésiennes), même en présence de conflits directionnels importants entre les deux modalités. Les participants arrivaient significativement mieux à discriminer les amplitudes de deux rotations consécutives quand on leur présentait les deux signaux simultanément, par rapport à la présentation de chaque modalité séparément (Etude 1). Notre recherche démontre également que les patients avec un déficit vestibulaire unilatéral intègrent eux aussi les signaux visuo-vestibulaires d'une façon optimale (Etude 2). La deuxième partie du présent travail examinait les interactions vestibulo-somatosensorielles. Nous montrons que l'information vestibulaire sous forme de rotations passives augmente la sensitivité tactile au niveau des doigts, comparé à une condition contrôle statique (Etude 3). Cet effet de la stimulation vestibulaire sur le toucher n'est pas directe mais dépend de la présence d'information visuelle sur le mouvement de soi: d'abord les signaux visuels et vestibulaires sont combinés et c'est ce percept intégré qui influe sur la sensitivité tactile (Etude 4). Dans la troisième partie, nous avons étudié l'influence des signaux vestibulaires sur l'attention et la conscience visuelles. La stimulation vestibulaire oriente l'attention d'une façon exogène, mais seulement à des latences très courtes à partir du début de la stimulation. Cette influence est plus robuste et présente pendant toute la durée de la stimulation quand le signal vestibulaire oriente attention d'une façon endogène (Etude 5). La stimulation vestibulaire affecte également la conscience visuelle. En utilisant le paradigme de la suppression continue par flash pour réprimer un flux optique pendant des rotations passives, nous démontrons que les participants deviennent conscients plus rapidement du flux optique qui simule une rotation dans une direction congruente à la rotation vestibulaire par rapport au flux optique dans une direction incongruente (Etude 6). En conclusion, nos travaux sont pertinents pour le domaine de la recherche multisensorielle en générale, et, plus particulièrement, pour la recherche sur le système vestibulaire et ses interactions avec d'autres sens. Nous mettons en évidence comment les signaux vestibulaires, visuels, proprioceptifs et somatosensoriels sont combinés par le cerveau afin de construire une représentation cohérente de soi dans l'espace.

Mots-clefs : vestibulaire, multisensoriel, intégration visuo-vestibulaire, déficit vestibulaire unilatéral, sensitivité tactile, attention visuelle, conscience visuelle

Introduction

Overview

Vestibular research has expanded substantially in the last decades, refining the anatomical pathways and mechanisms by which vestibular information is processed, but also its functional relevance for several behaviours. We now know that vestibular information is processed in tight proximity with other senses, allowing for self-motion detection, balance maintenance, spatial navigation and even self-perception. The study of the vestibular system is thus not only important for understanding its anatomical and functional organization in cortical and subcortical structures, its disorders and elaborating more precise diagnostic and therapeutic approaches, but also for a more general understanding of behaviour and the self, based on the perception of the body and of the body in space. The present thesis will demonstrate that for this it is important to gain a deeper insight into how vestibular information interacts with other senses, such as vision, touch, proprioception and pain, underlying the more complex functions.

The present thesis examined the interaction of vestibular information with visual and somatosensory cues, as well as the influence of vestibular information on cognition (visual attention) and consciousness (visual awareness). In the **introduction** we give a brief overview of the neuroanatomy of the vestibular system, the methods used to study it, as well as the current knowledge about the interplay of the vestibular sense with vision and touch and its influence on higher-order cognitive functions. In **Part 1**, we describe our work on visuo-vestibular integration. Study 1 deals with the integration of conflicting visuo-vestibular cues, highlighting the strength of the interaction between these two senses, as we show optimal integration for visual and vestibular cues each signalling self-motion around a different axis. Study 2 demonstrates that patients with unilateral vestibular loss (UVL) also show optimal visuo-vestibular integration, despite previously reported difficulties of vestibular and visual motion processing in this clinical condition. **Part 2** of the present thesis is dedicated to vestibular-somatosensory interactions. In Study 3 we show that vestibular stimulation in the form of passive whole-body rotations increases tactile sensitivity to electrical stimuli applied at the finger tips. Study 4 refines and extends this finding and links it to work from Part 1 (visuo-vestibular integration), showing that vestibular effects on touch occur after vestibular information is combined with visual cues. **Part 3** of this thesis examined the influence of vestibular information on cognitive processing beyond multisensory integration (Parts 1 and 2). In Study 5 we show that vestibular stimulation orients exogenous and endogenous visual attention in the direction of rotation. Study 6 explored the impact of vestibular stimulation on visual awareness, showing that participants are aware of a visual optic flow stimulus that is congruent with the direction of vestibular rotation faster, than of an optic flow stimulus that is incongruent with the direction of rotation. We bring together all of these findings and situate them in the frame of multisensory and vestibular research in the **general discussion** section. In particular, we will discuss how our behavioural results account for the laws of multisensory integration established through electrophysiological recordings in anesthetised animals, together with previous research in this domain. We will outline the role of each sensory cue during visuo-vestibular and visuo-vestibulo-tactile interactions, and propose experimental investigation of the neural correlates of such interaction. We shall conclude by highlighting issues to be addressed in future research.

Brief anatomy of the vestibular system

Located in the inner ear, the vestibular labyrinths are each composed of two otolith organs sensing linear accelerations and the position of the head with respect to gravity, and three nearly orthogonally situated semi-circular canals, responsible for detecting angular accelerations (Goldberg and Fernández 2000, Highstein, Fay et al. 2004). Each semi-circular canal is widened on one end, forming the ampulla, which contains vestibular hair cells. These biological sensors react to the displacement of the endolymph within the canals and thus transduce head motion into neural firing rate (Goldberg and Fernández 2000). From the inner ear the vestibular nerve projects to the vestibular nuclei, extensively connected with the cerebellum, and further projecting to the thalamus and, from there, to the cerebral cortex (Lopez and Blanke 2011). Already at the level of vestibular nuclei the distinction between active and passive head-movements is computed (Cullen, Roy et al. 2003, Roy and Cullen 2004). The vestibular system subtends three basic reflexes: the vestibular-ocular reflex (VOR), the vestibular-cervical reflex (VCR) and the vestibular-spinal reflex (VSR) (Mergner, Nardi et al. 1983, Tweed, Sievering et al. 1994, Mergner and Rosemeier 1998, Fetter 2007). The VOR is one of the fastest reflexes in humans and allows the stabilisation of the image on the retina during head motion by rotating the eyes to compensate for such motion. The VCR and VSR allow postural adjustment and compensatory head and body movements, for instance to prevent falls. Thus, the vestibular system underlies self-motion perception and balance maintenance.

The successful fulfilment of these functions is made possible through the very early convergence of vestibular information with the information from other sensory modalities, such as vision, somatosensation and proprioception. Animal studies have shown that vestibular nuclei neurons respond to visual optic flow stimuli as well as stimulation on the animal's paw (Magnin and Putkonen 1978). Multisensory responses are also present in the thalamus and the cortex (Waespe and Henn 1978, Meng and Angelaki 2010, Lopez and Blanke 2011). Unlike other sensory modalities, which project to a designated primary cortex, the so-called vestibular cortex is spread over multiple cortical areas (over 10 areas identified so far, (Lenggenhager and Lopez 2015)), spanning the somatosensory, insular and temporo-parietal regions (Figure 1) (Lopez and Blanke 2011). In non-human primates the core regions of the vestibular cortex are thought to be the parieto-insular vestibular cortex (PIVC) (Akbarian, Berndl et al. 1988, Grüsser, Pause et al. 1990, Grüsser, Pause et al. 1990, Guldin and Grüsser 1998), the ventral intraparietal area (VIP) (Bremmer, Klam et al. 2002, Schlack, Hoffmann et al. 2002) and the dorsal medial superior temporal area (MSTd) (Bremmer, Kubischik et al. 1999, Logan and Duffy 2006, Gu, Angelaki et al. 2008). Non-human primate studies have shown that some of these regions host bi- and even trimodal neurons, responding to passive self-motion, visual optic flow and tactile stimulation on the animal's face (Bremmer, Klam et al. 2002, Schlack, Hoffmann et al. 2002, Avillac, Hamed et al. 2007). It is important to note that PIVC is not merely connected to the other areas processing vestibular information, but also receives projections from many areas involved in coding of body-related information: the primary somatosensory cortex, posterior parietal cortex, premotor cortex, cingulate cortex (Guldin, Akbarian et al. 1992, Grüsser, Guldin et al. 1994); and it is thought to integrate signals from personal and extrapersonal spaces. Recent meta-analytical studies of human neuroimaging data employing different techniques of vestibular stimulation converge on the right parietal operculum region (as well as retroinsular cortex, and/or posterior

insula as the central area for the vestibular cortex (Lopez, Blanke et al. 2012, Zu Eulenburg, Caspers et al. 2012).

It is these multisensory properties of the vestibular system that we have behaviourally explored in the present thesis, seeking to refine the existing knowledge on visuo-vestibular, vestibular-tactile and trimodal visuo-vestibular-tactile interactions.
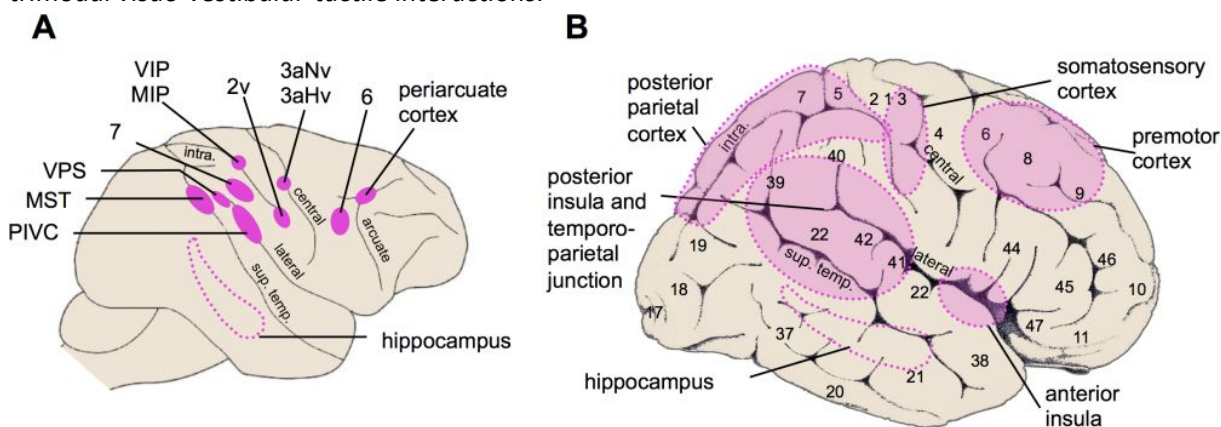

Figure 1. Main cortical vestibular areas in the primate (A) and human brain (B). (from LENGGENHAGER B. and LOPEZ C. (2015).

Experimental techniques for the study of the vestibular sense

Clinical experiments used to assess the integrity of the vestibular function proved to be useful for experimental exploration of vestibular contributions to cognition. Caloric vestibular stimulation (CVS) is such a technique during which cold (~20°C) or warm (~40°C) water or air is applied into the external auditory canal, which leads to the movement of the endolymph and consequently the modulation of the firing rate of the vestibular nerve, resulting in the activation of contralateral (for cold stimulation and ipsilateral for warm stimulation) subcortical and cortical vestibular structures. Spontaneous nystagmus arises about 20 seconds after the beginning of stimulation with the slow phase towards the irrigated ear (during cold stimulation), and is accompanied by dizziness (Freyss and Toupet 1978, Fasold, von Brevern et al. 2002, Ngo, Liu et al. 2007).

Galvanic vestibular stimulation (GVS), involves placing electrodes over the mastoid bones and passing a small current between them, producing a "galvanic body sway" in the direction determined by the polarity of the current. That is, anodal current decreases the firing rate of the vestibular afferents, whereas cathodal current increases it, subjects thus perceive sway towards the cathode, and compensate by swaying towards the anode and away from the cathode (Swaak and Oosterveld 1975, Fitzpatrick, Burke et al. 1994).

In line with animal studies, PET and fMRI imaging studies have shown these techniques to produce activations in the insular cortex and parietal operculum, superior temporal gyrus, and angular and supramarginal gyri. Vestibular activation was also reported in the primary and secondary somatosensory cortices, as well as the precuneus, cingulate cortex, frontal cortex, and hippocampus

(Bottini, Sterzi et al. 1994, Bottini, Paulesu et al. 1995, Lobel, Kleine et al. 1998, Bense, Stephan et al. 2001, Suzuki, Kitano et al. 2001, Dieterich, Bense et al. 2003, Indovina, Maffei et al. 2005, Eickhoff, Weiss et al. 2006).

Apart from the areas involved in the processing of vestibular information, both these stimulation techniques are thought to activate other structures as a result of concomitant non-vestibular sensations: e.g. pain, somatosensation, audition (Lopez, Blanke et al. 2012). The method of choice for vestibular research has thus become a motion platform, capable of delivering ecological translational and rotational vestibular stimuli. Such a platform provides natural 3D motion, and allows selective stimulation of the vestibular organs, e.g. a given pair of semi-circular canals. The intensity, the direction, as well as the duration of the stimulation can also be controlled in a precise manner.

This thesis examined multimodal vestibular interactions with other senses. To do so, we performed a series of studies using a custom-built rotation platform to deliver the vestibular stimulus in the form of passive whole-body rotations. Visual stimuli were delivered through a computer display, mounted on the platform, or a head-mounted display. For tactile stimuli, electrical or mechanical (solenoids) stimulation was applied at the fingers.

Visuo-vestibular perception and illusions

The vestibular system is tuned for self-motion detection. It appears, however, that this task is difficult to achieve without additional information. For example, low frequency vestibular stimuli are poorly encoded by the vestibular system (Waespe and Henn 1978, Probst, Straube et al. 1985). Moreover, constant velocity rotation in darkness ceases to be encoded by the vestibular organs about 20s after motion onset (Cohen, Henn et al. 1981, Bertolini, Ramat et al. 2011). When such motion is abruptly stopped an illusory and very compelling sensation of rotation in the opposite direction ensues (post-effect). It is possible to attain a more accurate estimation of self-motion and counter these shortcomings of the system through the combination of vestibular information with other senses, and first of all – vision. Visual information in the form of retinal optic flow accompanies most of our self-motions under normal conditions and is complementary to the vestibular sense, being most effective at coding changes in position and velocity, as well as low frequency low acceleration motion stimuli (Butler, Campos et al. 2014).

How do these two cues influence each other? A visual motion stimulus can cause a distinct sensation of self-motion, called vection (Berthoz, Pavard et al. 1975, Lestienne, Soechting et al. 1977). Vection can be illustrated by the compelling illusion occurring when one is sitting in a stationary train and a neighbouring train starts moving, producing the sensation, instead, that it is the train one is sitting in that started moving in the opposite direction (note that this illusion only occurs at slow velocity of the visual stimulus). Vestibular stimulation can induce illusory perceptions of visual stimuli presented during such stimulation – the so-called oculogyral illusion (an apparent motion of an actually stationary object) (Clark and Stewart 1969, Lackner and DiZio 2005). The study of visuo-vestibular interactions has been investigated intensively in animal and human studies (Waespe and Henn 1978, Waespe and Henn 1979, Schultheis and Robinson 1981, Baker, Wickland et al. 1987, Mendonça, Santos et al. 2011). Adaptation paradigms in different species have shown that conflicting visual and

vestibular stimuli exert mutual influence. For instance, if during passive self-motion around one axis an animal/human is exposed to visual optic flow around another axis, the VOR is modified and can even be cancelled out depending on the stimulation (Trillenberg, Shelhamer et al. 2003). In humans, subjective self-motion perception is also affected: when passively being rotated clockwise around the yaw axis and simultaneously receiving a clockwise rotation visual stimulus, the two cues are indicating mutually exclusive self-motion directions (Ishida, Fushiki et al. 2008). However, it was shown that this conflict is resolved by attributing more weight to the visual stimulus – i.e. the perceived rotation direction will become the one mostly indicated by the visual optic flow.

Our own pilot research has shown that combining conflicting visual and vestibular stimuli can lead to intriguing perceptual illusions that appear strongly compelling to the subject. Participants were seated in the rotating chair. A virtual reality scene was created by placing a monitor above their knees displaying a virtual stereoscopic representation of their lower limbs superimposed onto a rotating realistic background floor (Figure 2, A). Left-right (60° at 0.125 Hz and 45° at 0.25 Hz) sinusoidal rotations were delivered while participants were observing the 3D scene in total darkness. Visuo-vestibular conflict was achieved by manipulating the direction of rotation of the virtual floor: it rotated either in the opposite direction to the participant (congruent condition) or in the same direction (incongruent condition). In accordance with previous research our participants (N=10) also exhibited a switch in the direction of perceived motion as dictated by the visual scene in the incongruent condition. However, they also reported illusory trajectories (Figure 2, B: a, b, c and d) present only in one incongruent condition (60°, 0.125 Hz) that are not explained by visual dominance alone. There might thus exist wide individual differences in the perceived subjective motion pointing towards the need for a more precise study of the phenomenology of vestibular illusions.
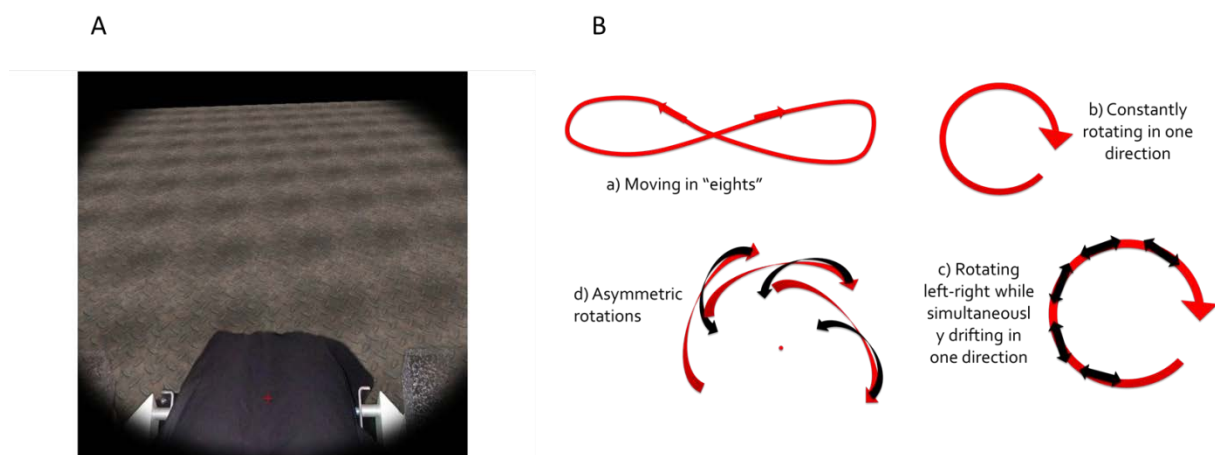
Figure 2. A: Virtual reality setup, showing the rotating platform, participants' legs, and a virtual floor. B: self-motion patterns described by the participants.

In a subsequent group of pilot experiments we quantified another aspect of visuo-vestibular interactions: speed perception. We explored whether presenting vestibular stimulation along with slower-speed visual optic flow would reduce the perceived velocity of self-motion.

In Experiment 1, participants (N=15, 24.04, SD=4.8, 4 females) judged the perceived speed of their displacement on a scale from 0 to 100. At the beginning of the experiment they were exposed to four

100°/s rotations (two clockwise, two counter clockwise) as the maximal reference point, and then completed 4 training trials. After each rotation, they had 5s to report the speed using a joystick to move a cursor on the horizontal scale displaying only the bounding values (0 and 100). On every trial the cursor appeared at 0 (left end). Three vestibular speeds were used (30, 60, 90°/s), each in conjunction with either same speed congruent optic flow (e.g. 30°/s vestibular rotation clockwise paired with 30°/s optic flow counter clockwise), 10°/s optic flow in a congruent direction, and 10°/s optic flow in the incongruent direction. There were thus nine experimental conditions each repeated 20 times. The motion of the chair and the motion of the optic flow were synchronised in time. The experiment was divided into four blocks (~5min each). The same number of clockwise and counter clockwise rotations was used.

Experiment 2 was based on Experiment 1. A different set of conditions was tested. Participants (N=14, 26.1, SD=4.2, 2 females) were exposed to one vestibular speed of 90°/s in conjunction with either of four visual speeds (10, 30, 45 and 90°/s), in either congruent or incongruent directions (the 90°/s speed was presented only in the congruent direction). A vestibular only condition was also tested (no optic flow was presented). There were thus eight conditions repeated 20 times.

A 3 x 3 repeated measures ANOVA with factors Optic flow (congruent 10°/s, incongruent 10°/s and congruent same speed as vestibular) and Chair rotation speed (30°/s, 60°/s, 90°/s) was performed on participants' mean estimates in Experiment 1. It revealed the two main effects and the interaction to be significant (Optic flow $F_{(2, 28)}=67.098$, $p<0.0001$; Chair rotation speed $F_{(2, 28)}=111.31$, $p<0.0001$; interaction $F_{(4, 56)}=6.5803$, $p=0.00021$). Post-hoc Bonferroni-corrected t-tests showed for each chair rotation speed no differences between congruent and incongruent directions of 10°/s optic flow ($p=1$), both being always judged as significantly slower than rotations with the same speed of optic flow (all $p<0.0001$). 30°/s chair speed rotations were judged as slower than 60°/s rotations, and the latter – slower than 90°/s rotations (all $p<0.0001$) (Figure 3, A).

As the design of Experiment 2 was not balanced, we used planned t-test Bonferroni-corrected comparisons. Nine comparisons were performed ($p= 0.006$). No significant differences were found between congruent and incongruent optic flow at 10°/s ($p=0.5$) and 30°/s ($p=0.02$), but 45°/s incongruent optic flow was judged as significantly faster ($p=0.002$) than 45°/s congruent flow. Congruent flow at 10°/s was not significantly different from 30°/s flow (trend: $p=0.007$), but 30°/s congruent flow was significantly slower than 45°/s congruent flow ($p=0.005$). Incongruent flow was always judged as significantly faster with increased flow velocity ($p=0.0001$, and $p=0.002$, accordingly). 90°/s congruent optic flow was judged as significantly faster than the no flow condition ($p=0.005$) (Figure 3, B).
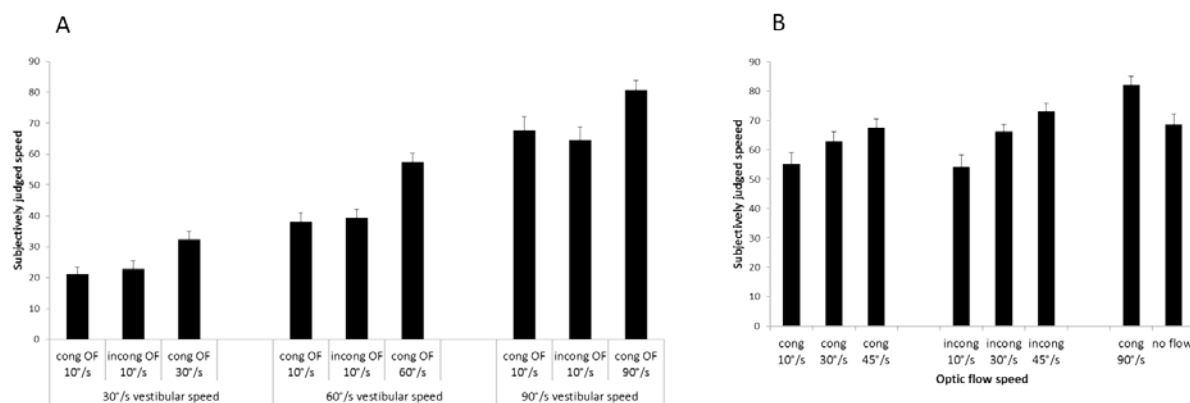
Figure 3. Participants judgments of perceived self-motion speed (scale from 0 to 100). A: Three vestibular velocities were used (30, 60, 90°/s) in conjunction with 10°/s congruent or incongruent optic flow, as well as same speed congruent optic flow (OF). B: One vestibular velocity (90°/s) was used in conjunction with 10, 30 and 45°/s optic flow in congruent or incongruent directions, as well as 90°/s congruent optic flow and no optic flow.

The pilot Experiments 1 and 2 showed that for slow velocity optic flow there was no difference between congruent and incongruent directions, independently of the chair speed, whereas for higher optic flow velocity (i.e. 45°/s) congruent optic flow was judged as slower than incongruent optic flow. This effect may be attributed to attentional processes, whereby attention, and possibly arousal, is higher during higher-speed stimuli, making the distinction between congruent and incongruent cues more fine-grained. Additionally, there might be some limits of multisensory integration of conflicting information: faster optic flow in an incongruent direction to the vestibular signal is an unnatural stimulus and may bias the system towards attributing more weight to the complementary vestibular modality. The presence of the same speed optic flow also increased the perceived speed of rotation in comparison to a no flow condition at 90°/s chair velocity (which also means that the speed of rotation in the visuo-vestibular combined condition was closer to the correct estimate, as multisensory integration would predict). These findings corroborate and refine the previously reported visual dominance in the perception of self-motion, and allowed us to conduct the experiments described in **Part 2, Study 4** of the present thesis.

Visuo-vestibular integration

A well-established feature of human perception is that when perceiving the environment or one's own body, instead of discarding redundant sensory information, observers most often combine it in order to form more reliable percepts (visuo-vestibular integration: Prsa, Gale, and Blanke 2012; Fetsch et al. 2009; Butler et al. 2010; Gu, Angelaki, and Deangelis 2008; visuo-auditory integration: Parise, Spence, and Ernst 2012; Alais and Burr 2004; Mendonça, Santos, and López-Moliner 2011; visuo-proprioceptive: van Beers, Sittig, and Denier van der Gon 1996; van Beers, Sittig, and Denier van der Gon 1999, Marc O Ernst and Banks 2002; visual and visuo-tactile integration: Hillis et al. 2002). Bayesian statistics of sensory cue combination constitutes the modern framework for studying human and animal perception and can account for psychophysical performance in multisensory

integration tasks. Accordingly, it is assumed that perceptual estimates are uncertain and therefore probabilistic (Knill and Pouget 2004; Ernst and Banks, 2002), in the sense that repeated estimations of the same stimulus are variable from trial to trial. This variance embodies the perceptual uncertainty associated with the sensory cue (due to noisy sensory and neural processing), which is reduced according to statistical optimality when multiple uncertain estimates of the same physical property are probabilistically combined (Ernst and Banks 2002).

Vestibular and visual cues have been shown to integrate optimally during passive whole body translations and rotations, that is, participants were more accurate in judging the amount of self-motion in the presence of both the visual and the vestibular cues, as compared to just one of these modalities (Fetsch, Turner et al. 2009, Butler, Smith et al. 2010, Prsa, Gale et al. 2012). The principles of multisensory integration state that for maximal multisensory integration to occur, the events in the two modalities should co-occur temporally and spatially (Stein, Scott Huneycutt et al. 1988, Stein 2012, Fetsch, DeAngelis et al. 2013). However, these rules, based on electrophysiological animal recordings, do not seem to be ubiquitous when addressing behaviour. For example, many illusory percepts are based on the convergence of conflicting multisensory information. Visual "capture" of sound gives rise to the "ventriloquist effect", where sound is perceived to emanate from a given visual stimulus rather than from its actual auditory source (Stein, 2012). The same holds for visuo-proprioceptive interactions in the "rubber hand illusion": participants feel a fake hand as their own when they see it being stroked while simultaneously being stroked on their (hidden) real hand (Botvinick and Cohen, 1998).

Study 1 *of the first part of this thesis addresses the spatial rule for visuo-vestibular stimuli for self-motion: is multisensory integration possible and if so, can it be optimal, when the two cues specify rotation around a different axis. This experiment shows, that despite such large spatial conflicts, participants optimally integrate visuo-vestibular cue pairs.*

Another important rule in multisensory research is the principle of "inverse effectiveness". According to this principle, when individual cues only weakly activate a neuron, the multisensory response enhancement will be proportionately larger (Stanford, Quessy et al. 2005, Stein 2012, Fetsch, DeAngelis et al. 2013). We explored this effect for visuo-vestibular integration in Study 2 of the first part of the present thesis in a cohort of patients with unilateral vestibular loss (UVL).

Behaviourally, patients with unilateral vestibular lesions have a decreased ability in discriminating the direction of passive rotations based on vestibular stimulation (Cutfield, Cousins et al. 2011, Jamali, Mitchell et al. 2014). In primates, this behavioural deficit is thought to be subtended by increased neuronal detection thresholds for self-motion in vestibular nuclei (Sadeghi, Chacron et al. 2007, Sadeghi, Minor et al. 2007). In addition, various animal studies show a diminished number of Type I neurons (those increasing firing rates during ipsilateral rotations) with decreased sensitivity to self-motion in the lateral and medial vestibular nuclei (for a review see (Smith and Curthoys 1989). Also, the rotational VOR is asymmetrical during passive vestibular stimulation (impaired in the ipsilesional horizontal and vertical planes) (Curthoys 2000, Deutschländer, Hüfner et al. 2008) and remains different between active and passive head motion (Black, Thurtell et al. 1999, Curthoys 2000). During optokinetic stimulation (moving visual environment) patients also show a decreased optokinetic nystagmus (Berthoz, Pavard et al. 1975, Lestienne, Soechting et al. 1977). Moreover, in bilateral vestibular loss visual motion is detected with longer latencies and patients with UVL show a

cortical suppression for the processing of visual motion (Deutschländer, Hüfner et al. 2008, Valko, Lewis et al. 2012). Moreover, patients with UVL show a long-term (still present one year postoperatively) deficit in the dynamic visual vertical (the visual vertical perceived during concomitant optokinetic stimulation in the roll plane) (Lopez, Borel et al. 2005, Lopez, Lacour et al. 2007). Previous research also points to abnormal multisensory integration in patients with UVL. Postural control is one example requiring successful integration of vestibular, visual and proprioceptive information. In patients with UVL, performing a dual task causes strong interference in postural control, and vice versa, and secondary task performance is impaired during induced postural instability, which has been interpreted as evidence for enhanced cognitive requirement during visuo-vestibular integration in such patients (Kristinsdottir 2001, Redfern, Jennings et al. 2001, Redfern, Talkowski et al. 2004). Spatial navigation (and more precisely, path integration) is also impaired in such patients in the presence of visual and vestibular information and during complex navigating tasks having higher spatial processing requirements, such as reversing or shortcutting a path (Péruch, Borel et al. 2005, Borel, Lopez et al. 2008, Dieterich and Brandt 2015). This suggests an impairment in the construction of adequate internal spatial representations which relies on the integration of visual and vestibular information. Finally, during passive self-motion, while having to fixate or in darkness, patients with unilateral vestibular damage were more impaired than controls on a secondary task, again implying a cognitive cost attributed by the authors to the necessity of maintaining compensation for the vestibular loss (Redfern, Talkowski et al. 2004, Talkowski, Redfern et al. 2005). Additionally, simply having to fixate or perform smooth pursuit degraded patients' performance on a secondary task (Yardley, Gardner et al. 1999). It thus appears that - despite a certain level of compensation - patients with UVL experience difficulties in self-motion processing based both on vestibular and visual information, with underlying brainstem and cortical changes that persist over one year post-operatively.

*We explored whether patients exhibit multisensory visuo-vestibular integration, and if so, whether it is optimal and, in addition, more pronounced on the side of the lesion (**Part 1, Study 2** of the present thesis).*

Vestibular-somatosensory interactions

As already described above, together with somatosensation the vestibular system is crucial for the maintenance of balance and postural stability. Previous research has shown that both systems overlap at several neuroanatomical levels. Vestibular nuclei in the cat have been shown to respond to somatosensory stimulation on the animal's paw (Magnin and Putkonen 1978). The descending (DVN), superior (SVN) and medial (MVN) vestibular nuclei project to thalamic nuclei (ventral posterior lateral nucleus (VPL) and nucleus ventralis intermedius (Vim)) that are all known to relay somatosensory information to the primary somatosensory areas areas 3a, 3b and 1 and secondary somatosensory areas in different species, as well as non-human and human primates (Büttner and Henn 1976, Blum, Day et al. 1979, Marlinski and McCrea 2008, Lopez and Blanke 2011). At the level of the cortex, vestibular projections to the arm area 3a and area 2v in the primary somatosensory cortex were found in squirrel and rhesus monkeys (interestingly, visual optic flow stimuli also activate area 2v) (Fredrickson, Figge et al. 1966, Ödkvist, Schwarz et al. 1974, Büttner and Buettner

1978). Stimulating the vestibular nerve results in cortical potentials at the level of the area 2v, a region partially overlapping with the primary somatosensory cortex. Interestingly, this area was also activated by median nerve stimulation.

Behavioural evidence for vestibulo-somatosensory interaction comes from patient studies. Left ear cold CVS temporarily reduces hemianesthesia in right and left brain-damages patients (importantly, however, right cold CVS does not produce this effect for right hemianesthesia in left-damaged patients) (Vallar, Sterzi et al. 1990, Vallar, Bottini et al. 1993, Bottini, Paulesu et al. 2005). Right warm CVS also leads to the recovery of left hemianesthesia in right brain-damaged patients (Vallar, Sterzi et al. 1990). This reduction of tactile imperception speaks for the dominant role of the right hemisphere in processing bodily related information. The effect is thought to occur through the activation of right somatosensory areas (and more precisely, the secondary somatosensory cortex), probably hosting neurons with ipsilateral receptive fields (Bottini, Paulesu et al. 2005). It is also considered to occur independently from the direction of reflexive eye-movements induced by CVS, as, for example, blind-folded patients also exhibited a reduction of hemianesthesia (Vallar, Sterzi et al. 1990). It is also unlikely that the improvement of tactile perception is brought about by attentional mechanisms, whereby attention would be oriented in the direction of the ear stimulated by CVS, because left CVS gives rise to improvement of both right and left hemianesthesia (Bottini, Gandola et al. 2013).

Similar results have been obtained with healthy subjects, and the findings of these studies also support the specificity of the increase in tactile sensitivity as opposed to attentional effects (see below for more detailed introduction). In healthy subjects the perception of near-threshold tactile stimuli on the fingers was improved during CVS and GVS (Ferrè, Bottini et al. 2011, Ferrè, Sedda et al. 2011). Left cold CVS also has a differential effect on touch and pain: while increasing tactile sensitivity it decreases sensitivity to painful stimuli (Ferrè, Bottini et al. 2013). In addition, left cold CVS selectively has been reported to enhance the N80 somatosensory evoked potential component (induced by left median nerve stimulation) which is thought to be generated in the parietal operculum – the centre of vestibular cortical processing (Ferrè, Sedda et al. 2011).

*In the present thesis we explored vestibular and visuo-vestibular effects on touch (**Part 2**). In **Study 3** participants received mild tactile stimuli on their fingertips during ipsilateral or contralateral rotation or while being stationary. This manipulation allowed us to further address possible attentional effects of vestibular stimulation on tactile processing. Taking it further, in **Study 4**, we explored whether the facilitatory effect of vestibular stimulation on touch is direct or would be modulated by concurrent visual information. We repeated the protocol from **Study 3** adding a new condition: vestibular stimulation in the presence of slower-speed optic flow that produced a subjective sensation of slow motion (using the setup described above in section 2.1.). This manipulation allowed us to demonstrate that visuo-vestibular interactions precede vestibular-tactile effects.*

Vestibular contributions to cognition

In its final part (**Part 3**) this thesis addresses the role of vestibular information in higher-order cognition. The role of the vestibular system in our daily life is not limited to lower-level sensory interactions. Through the lower-level interplay with other sensory modalities vestibular information

influences space and own-body perception , as well as the perception of one's body in space, and is even thought to impact on social cognition (Mergner and Rosemeier 1998; Ferrè et al., 2013; Lopez et al., 2008; Lenggenhager and Lopez 2015).

Clinical reports have described vestibular patients as presenting with distortions in the perception of body parts ("neck swelling", "feet seem to elongate", "hands became larger and moved in different directions") during episodes of dizziness (Bonnier 1905, Lopez 2013). Experimentally, CVS induced changes in perceived tactile stimuli on the hand's surface (distance between stimuli perceived as longer) as well as changes in the perceived metrics of the hand. In these experiments participants had to point to anatomical landmarks on their occluded hand during CVS and SHAM stimulation. Both length and width judgements were increased during CVS, speaking for a vestibular contribution to the body-schema (Lopez, Schreyer et al. 2012).

Vestibular stimulation also influences ownership for body parts, as shown by the rubber hand illusion (RHI) paradigm. During GVS stimulation subjective ratings on the ownership of the rubber hand were increased, and hand localisation judgements were more biased in the direction of the rubber hand (proprioceptive drift) (Lopez, Lenggenhager et al. 2010). However, opposite results have also been observed, where GVS decreased the localisation bias towards the rubber hand. Here the authors claim that as GVS increases somatosensation, it could boost the somatosensory/proprioceptive component of bodily awareness thus making one more resistant to visual capture underlying the RHI effect (Ferrè, Berlot et al. 2015).

Further evidence of vestibular contribution to own body perception comes from amputee patients. CVS transiently restores abnormal (telescoped) phantom limbs to their normal length and alleviates the pain in painful phantom sensations (André, Martinet et al. 2001, Miller and Ngo 2007). Electrical stimulation of the temporo-parietal junction, one of the regions of the so-called vestibular cortex, has been reported to induce out-of-body experiences (OBE), whereby the patient perceived herself floating above her bed, looking down at her own body (Blanke, Ortigue et al. 2002). OBEs are reported to have an important vestibular component, being accompanied by vestibular illusions of flying, floating, projection, rotation and limb motion (Cheyne and Girard 2009). Other clinical conditions point towards the importance of vestibular information for the bodily self. Depersonalisation disorder is a condition characterised by a feeling of being detached from the self and the environment (Simeon 2004). Such feelings of unreality have been reported in healthy subjects undergoing CVS and vestibular patients, those with recent balance problems reporting more detachment from reality symptoms than patients without such recent problems (Sang, Jauregui-Renaud et al. 2006, Jáuregui-Renaud, Sang et al. 2008, Kolev, Georgieva-Zhostova et al. 2014).

Evidence for vestibular influence on space perception comes from clinical as well as experimental data. CVS transiently reduces vsiuo-spatial neglect in brain damaged patients (Rubens 1985, Bottini, Karnath et al. 2001). Patients with vestibular dysfunctions sometimes present with the "room-tilt illusion" whereby the visual surrounding is suddenly rotated 90° or 180° around the stationary patient (Tiliket, Ventre-Dominey et al. 1996, Brandt, Strupp et al. 2014). A similar effect is observed in microgravity: the inversion illusion – the observer perceives him/herself rotated in a stable environment (Lopez, Halje et al. 2008). Patients with bilateral vestibular loss exhibit difficulties in egocentric and object-based mental transformations (Grabherr, Cuffel et al. 2011). CVS was shown to selectively improve the speed of egocentric mental transformations (but not mental rotation of

letters or body parts) in healthy volunteers (Falconer and Mast 2012). Both CVS and vestibular stimulation using a rotating platform were shown to affect the perception of bistable images (Miller and Ngo 2007, Ngo, Liu et al. 2007, van Elk and Blanke 2012). Several studies have also examined vestibular effects on attention. Different kinds of vestibular stimulation were successfully used to orient attention in several tasks: the temporal order judgement task (TOJ)(e.g. Rorden, Karnath, & Driver, 2001), line bisection (e.g. Ferrè et al., 2013), mental number line (Hartmann, Grabherr, & Mast, 2012) and sound localisation (Lewald & Karnath, 2001).

In terms of the importance of vestibular signals for social cognition, there is evidence that vestibular otolith signals are used to extract important visual information regarding human posture and kinematics as well as facial features (Lobmaier and Mast 2007, Lopez, Bachofner et al. 2009, Deroualle and Lopez 2014). During self-motion perception (in the form of passive self-motion on a motion platform) while observing a moving image of self or of another person, the detection of motion onset is influenced by the identity of the seen image (Lopez, Falconer et al. 2013). Finally, during passive self-motion on a platform, self-identification with a mannequin is increased when it moves in synchrony with the self (Macauda, Bertolini et al. 2014).

Taken together these observations point to the prominent role of vestibular information in the perception of the body of oneself and others as well as spatial cognition. They also show that cross-modal interaction between vestibular cues and other senses take place in a similar way as described for non-vestibular multisensory interactions. For instance, auditory and tactile stimuli have previously been shown to orient visual attention (Driver and Spence 1998, Spence and Driver 2004). In the domain of awareness, similar cross-modal interactions were observed. For example, in a binocular rivalry paradigm (BR) Conrad and colleagues (Conrad, Bartels et al. 2010) presented two different visual stimuli to the two eyes and simultaneously participants could explore a tactile stimulus that was the same as one of the visual stimuli. The authors show, that dominance was prolonged and suppression was shortened for the visual stimulus that was congruent with tactile stimulus. In a similar BR paradigm motion sounds prolonged the dominance periods of visual motion percepts, moving in congruent directions.

*In **Part 3** of this thesis we refine the present-day knowledge on vestibular impact on visual attention and awareness. In **Study 5**, we show that attention is successfully oriented in the direction of rotation but mostly so when explicitly made task-relevant. In the final **Study 6** we demonstrate that vestibular stimulation impacts visual awareness during a continuous flash suppression (CFS) task (optic flow stimuli, congruent with the direction of rotation, break suppression faster than rotation-incongruent optic flow).*

Personal contributions

Part 1. Visuo-vestibular integration

Study 1: Learning to integrate contradictory multisensory self-motion cue pairings.

Personal contribution: performed research, analyzed data, wrote the paper.

Learning to integrate contradictory multisensory self-motion cue pairings

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Kaliuzhna et al.

Humans integrate multisensory information to reduce perceptual uncertainty when perceiving the world and self. Integration fails, however, if a common causality is not attributed to the sensory signals, as would occur in conditions of spatiotemporal discrepancies. In the case of passive self-motion, visual and vestibular cues are integrated according to statistical optimality, yet the extent of cue conflicts that do not compromise this optimality is currently underexplored. Here, we investigate whether human subjects can learn to integrate two arbitrary, but co-occurring, visual and vestibular cues of self-motion. Participants made size comparisons between two successive whole-body rotations using only visual, only vestibular, and both modalities together. The vestibular stimulus provided a yaw self-rotation cue, the visual a roll (Experiment 1) or pitch (Experiment 2) rotation cue. Experimentally measured thresholds in the bimodal condition were compared with theoretical predictions derived from the single-cue thresholds. Our results show that human subjects combine and optimally integrate vestibular and visual information, each signaling self-motion around a different rotation axis (yaw vs. roll and yaw vs. pitch). This finding suggests that the experience of two temporally co-occurring but spatially unrelated self-motion cues leads to inferring a common cause for these two initially unrelated sources of information about self-motion. We discuss our results in terms of specific task demands, cross-modal adaptation, and spatial compatibility. The importance of these results for the understanding of bodily illusions is also discussed.

Introduction

During passive self-motion (be it heading or rotation), an observer derives the direction, speed, and distance traveled from an optimal combination of redundant information provided by different sensory cues: visual, vestibular, auditory, and tactile sensations (Gibson, 1950; Kapralos, Zikovitz, Jenkin, & Harris, 2004; Warren & Wertheim, 2014). To date, in order to account for such processes, Bayesian statistics of sensory cue combination have been used, which describe how the perceptual uncertainty associated with the sensory cues (due to noisy sensory and neural processing) is reduced according to statistical optimality when multiple uncertain estimates of the same physical property are probabilistically combined (Ernst & Banks, 2002).

Computational theories of multisensory integration posit integration when a common cause is inferred for the sensory cues (Körding et al., 2007; Parise, Spence, & Ernst, 2012; Shams & Beierholm, 2010). The probability of a common cause depends on how similar or correlated these cues are and on the observer's prior beliefs or knowledge about the possible common cause.

In everyday natural settings, visual and vestibular stimuli signaling self-motion are most likely congruent and highly correlated, which results in their integration and mandatory fusion even in the presence of slight cue conflicts (Butler, Smith, Campos, & Bülthoff, 2010; Fetsch, Turner, DeAngelis, & Angelaki, 2009; Jürgens & Becker, 2006; Prsa, Gale, & Blanke, 2012). Accordingly, it is also assumed that integration should break down if the conflict between the stimuli is too large, implying that they relate to different sources. Such latter conflicts could also mean that there is no correlation between stimuli. In the present study we address the limits of visuo-vestibular integration by testing spatially conflicting multisensory (visuo-vestibular) cues.

Previous work has shown that large degrees of consciously detectable directional conflict do not lead to integration of visual, vestibular, and proprioceptive self-motion cues (Ohmi, 1996). Similar results have been obtained for conflicting cues pertaining to external objects (Bertelson & Radeau, 1981; Gebhard & Mowbray, 1959; Gepshtein, Burge, Ernst, & Banks, 2005; Lunghi, Morrone, & Alais, 2014; Pick, Warren, & Hay, 1969; Recanzone, 2003; Welch & Warren, 1980). Specifically, it has been found that integration occurs for small degrees of conflict, whereas for larger degrees of conflict such interactions between the two modalities are no longer observed (Gepshtein et al., 2005; Roach, Heron, & McGraw, 2006; Wallace et al., 2004).

It has, however, also been shown that multisensory cues can influence one another despite the absence of perceptual unification. Participants who initially do not integrate arbitrary cue pairings may learn to combine them when these stimuli temporally co-occur over time (i.e., arbitrary but correlated stimuli; Bresciani et al., 2005; Ernst, 2007; Wozny & Shams, 2011). Additionally, the particular demands of the task an observer has to perform might influence the integration process (Roach et al., 2006). It therefore appears possible that multiple parameters of conflicting stimuli could be taken into account to determine whether integration occurs: the amount of conflict, the task at hand, and the amount of correlated stimulus characteristics. The exact contribution of each of these parameters to the integration process remains unknown.

In our previous work, we have demonstrated that human observers integrate congruent yaw visual and yaw vestibular rotation cues according to statistical optimality (Prsa et al., 2012). Here, with an identical experimental apparatus and task design, we address whether repeated exposure to overtly spatially incongruent (but correlated on other dimensions) multisensory self-motion stimuli (visual and vestibular) results in optimal cue integration. Our participants were exposed to whole-body yaw rotations in conjunction with temporally synchronized optic flow rotation around a different axis (roll, Experiment 1). We asked

Kaliuzhna et al.

them to compare the sizes of two successively experienced rotation angles, and determined probabilistic descriptions of their perceptual estimates. Obtained results reveal that the variance associated with these incongruent visual–vestibular cue pairings decreased over time and progressively approached the statistically optimal predictions derived from the variances of the single-cue estimates. We argue that our results can be accounted for by a progressively increasing probability of attributing a common cause to the two incongruent stimuli. Further evidence for such integration was found when simultaneously exposing participants to whole-body yaw rotations in conjunction with synchronized optic flow rotation around the pitch axis (Experiment 2), which resulted in integration optimality right from the onset. We discuss the implications of our finding in the context of multisensory integration, own-body perception, and vestibular symptoms in neurological patients.

Materials and methods

Participants

Eight healthy adults naïve to the purpose of the study with normal or corrected vision and no history of inner-ear disease participated in each experiment (Experiment 1: two women, mean age = 24 ± 2.7 years; Experiment 2: three women, mean age = 22 ± 3.9 years). Three participants from Experiment 1 also participated in Experiment 2. All participants gave informed consent and received monetary compensation at 20 CHF/h. The studies were approved by a local ethics committee and were conducted in accordance with the Declaration of Helsinki.

Optimal Bayesian Estimator (OBE) model

In perceiving a whole-body rotation of size S, each sensory modality provides an independent estimate of S. Perceptual uncertainty is naturally associated with each of the unimodal estimates, the visual and the vestibular in our case, and can be measured as their trial-by-trial variance σ_{vi}^2 and σ_{ve}^2, respectively. Maximum likelihood estimation (derived from Bayes's rule) dictates that if the two unimodal cues are integrated according to statistical optimality, the uncertainty associated with the bimodal estimate σ_{bi}^2 is reduced relative to unimodal uncertainties according to

$$\sigma_{bi}^2 = \frac{\sigma_{vi}^2 \sigma_{ve}^2}{\sigma_{vi}^2 + \sigma_{ve}^2}. \tag{1}$$

Experimental setup

Subjects were seated in a centrifuge cockpit-style chair which delivered passive whole-body rotational stimuli (Figure 1). After adopting a comfortable position, the subjects were restrained by a five-point racing harness, foot straps, and extra cushioning. To prevent the subject's head from moving, a chin rest and a head fixation at the forehead were used.

The chair was digitally servo controlled (PCI-7352) and had very precise positioning of around 0.1°. The chair always rotated in the yaw plane and was centered on the rotation axis, restricting the vestibular stimuli to angular accelerations only. The rotation profiles of the chair were preset and designated the immediate angular position of the chair at a rate of 100 Hz. The velocity profile $v(t)$ of the rotations was a single cycle of a 0.77-Hz raised cosine function:

$$v(t) = \frac{A}{T}\left[1 - \cos\left(\frac{2\pi t}{T}\right)\right], \tag{2}$$

where A is rotation size and T is duration ($T = 1.3$ s in this case). Instantaneous angular position $p(t)$ was then specified as

$$p(t) = A\left[\frac{t}{T} - \frac{1}{2\pi}\sin\left(\frac{2\pi t}{T}\right)\right]. \tag{3}$$

The visual stimuli were presented on a 22-in. display, which was fixed to the chair in front of the subject at a distance of about 29 cm. The limited visual field covered ~80° of horizontal and 56° of vertical visual angle. The visual image consisted of a stereoscopic pattern of randomly distributed moving dots of different sizes. The dots were two-dimensional symmetric grayscale Gaussian blobs with a minimum and maximum standard deviation of 0.5 and 3 pixels, respectively. For each blob, the standard deviation was drawn from an exponential distribution with a rate parameter of 2, and the peak pixel intensity from a uniform distribution between 0.1 and 0.3 (1 denotes maximum intensity, i.e., white). The binocular disparity was a linear function of blob standard deviation and yielded minimum and maximum values of 0 (for the maximum-sized dots) and 50 (for the minimum-sized dots) pixels, respectively. All dots had therefore zero or positive stereoscopic depth. The dot density was set to 0.002 dots/pixel, producing roughly 3,500 dots in any given frame of the 1680 × 1050 resolution display. Their lifetime was not limited and their initial position reset at the start of every trial.

Rotation was simulated by placing the subject's viewpoint in the middle of the scene and rotating it around either the roll axis (Experiment 1) or the pitch axis (Experiment 2). These patterns simulated the actual optic flow that would result from physically
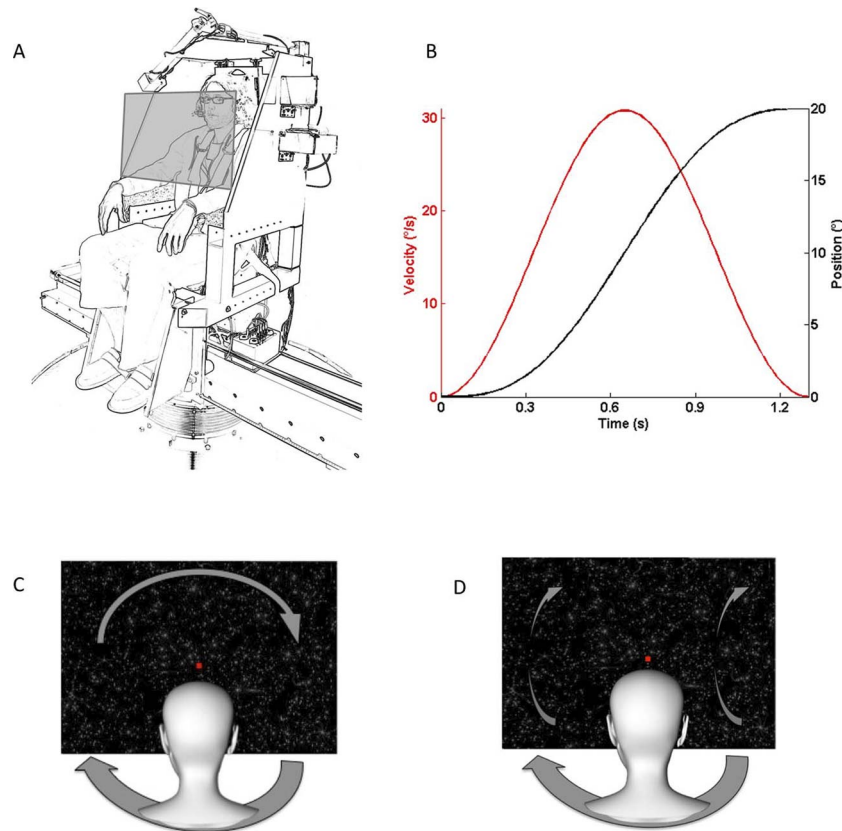
Figure 1. Experimental setup and experimental conditions. (A) Experimental setup. Participants were seated in a human motion platform that delivered yaw whole-body rotations. A 3-D monitor was positioned in front of the participant and showed a pattern of stereoscopic moving dots that simulated a visual stimulus which would result from actual whole-body rotations. (B) Position and velocity profiles of the rotation stimulus. (C) In Experiment 1, inertial motion around the yaw axis was paired with a visual motion stimulus signaling roll rotation. (D) Whole-body yaw rotations were paired with a visual rotational pitch stimulus in Experiment 2.

rotating the subject around these axes in congruent directions. During the rotations in all conditions, subjects were instructed to fixate a stationary central point, which was a filled red circle with a radius of 3 pixels and an intensity level of 0.5 presented at zero binocular disparity. The stereoscopic stimulus was generated by the Nvidia Quadro FX 3800 graphics card using the OpenGL quad-buffer mechanism. The stimulus was programmed with the Python language and viewed with the Nvidia 3D Vision kit (active shutter glasses) paired with a Samsung SyncMaster 2233RZ display (120-Hz refresh rate) via an infrared transmitter. The velocity of the optic flow matched that of the rotating chair. While subjects performed the task, masking white noise was presented over headphones.

Experimental paradigm

Subjects were seated in the rotating chair with a computer screen in front of them. On every trial they experienced two successive rotations (a standard and a test) and had to judge their relative size. The rotations were either delivered by the chair alone, simulated by the motion of the visual field on the display, or a combination of both (on every trial, the two rotations were of the same kind). The size of one of the two rotations was always 20° (i.e., the standard rotation), and the size of the second (i.e., the test rotation) was one of second equally spaced angles in the interval of 12°–27° tested using the method of constant stimuli (see Prsa et al., 2012, for a similar procedure). The two rotations were preceded, followed, and separated by an interval of 0.5 s. A 2-s period followed during which the subjects had to answer, via a button press, whether the second rotation was bigger or smaller than the first. The standard rotation was randomly assigned to come either first or second.

Subjects came in on two different days. On the first day we determined their unimodal discrimination thresholds (see Data analysis) for the vestibular and the visual modalities separately. In Experiment 1, participants performed the same task described previously for vestibular yaw rotations and visual roll rotations. In Experiment 2, the same task was performed, but with

Kaliuzhna et al.

vestibular yaw and visual pitch rotations. Participants first completed several blocks of vestibular-only stimuli, where the different test angles were presented in a randomized order. Each block contained 35 trials and lasted for about 5 min. Participants performed a minimum of 280 trials (in total), amounting to 40 trials per test angle. After extracting participants' thresholds for the vestibular modality, we used the same procedure for the visual modality. In order to match participants' visual thresholds to their vestibular thresholds, we manipulated the reliability of the visual stimulus by changing the coherence of the visual motion (number of dots simulating rotation or moving randomly). The random dots moved in a straight line with the identical displacement velocity profile as the rotation. The overall displacement size was limited to 200 pixels in horizontal and vertical directions and was drawn from a uniform distribution. The radial motion direction was randomly chosen for each dot between −180° and 180° (uniform distribution). The random dots were also Gaussian blobs with identical parameters and therefore were visually indistinguishable (when stationary) from the blobs simulating rotation. Their initial positions were also reset at the start of each trial and their binocular disparity remained constant. Participants performed a minimum of four visual-only blocks (140 trials, 20 trials per test angle) with a given level of coherence. If their performance matched that on the vestibular modality, this level of coherence was retained; otherwise it was changed and the procedure continued as described until a matched level was obtained. The experimentally established levels of visual coherence corresponding to matched discrimination thresholds in the two single modalities were then used for Experiment 1; they were 100% for four subjects, 95% for one subject, 85% for two subjects, and 80% for one subject. Analogously, for Experiment 2 the levels used were 100% for three subjects, 95% for three subjects, and 85% for two subjects. Overall, subjects performed a mean of 557.5 trials for each modality (about 40 repetitions of each test angle for each modality).

On the second day, subjects performed the task but were now exposed to the three conditions: unimodal vestibular, unimodal visual, and both modalities together. For bimodal comparisons, visual and vestibular stimuli were temporally synchronized and occurred simultaneously (e.g., Prsa et al., 2012). The experiment was divided into sessions of approximately 5 min that we grouped into six blocks (the comparisons between these blocks allowed us to test for progressive learning of the visuo-vestibular association). Every session contained trials of each of the three conditions presented in a randomized order, which made it impossible to predict which condition would occur next. Subjects performed a total of 420 trials for each of the three conditions: 70 trials per block per condition, 10 trials per test angle per

condition (i.e., 60 trials per test angle for each of the conditions). The direction of rotation (left or right for vestibular yaw and visual roll; up or down for pitch) was randomly chosen on each trial. In Experiment 1, left yaw rotations were always arbitrarily paired with right visual roll rotations (i.e., simulating a left roll self-rotation) and right yaw rotations with left visual roll rotations. In Experiment 2, left yaw was always arbitrarily paired with down visual pitch rotations (and right yaw rotations with up pitch rotations).

Data analysis

The data analysis was done using custom programs compiled in MATLAB (MathWorks). During the pretest, in order to match performance between the two modalities, we pooled the answers obtained for each test angle separately for the vestibular and visual conditions. For the analysis, the test angle was always compared to the standard angle, regardless of their order of occurrence in a trial. The proportion of "bigger" responses was calculated and fitted with a cumulative Gaussian function. From this fit we obtained discrimination thresholds for the two modalities. In order to match these thresholds, we manipulated the reliability of the visual cue as described earlier.

The analysis for the actual experiments was run in a similar fashion. Answers obtained for each test angle were pooled across all subjects to obtain a probabilistic measure and create a sufficient sample set for statistical comparisons. From the variance of the Gaussian fits to the proportion of "bigger" answers we obtained the measure of the discrimination threshold for each of the three conditions. We next conducted a bootstrap analysis to compare the predictions of the optimal observer model to the experimentally obtained values. To this end, we repeated the data fit for each condition 9,999 times, using a different subset of responses every time. The different subsets were formed by taking at random, with replacement, N trials from the total set of N for each test angle. The standard deviation of 9,999 repeated measures is then the standard error of the measure obtained using the original data set. Statistical tests were made by assessing the amount of overlap between the bootstrap iterations of two measures. If the measure of interest is σ and σ^j_{ex} and σ^j_{pr} are its experimental and predicted estimates obtained from the jth bootstrap sample, then the one-tailed bootstrap probability of $\sigma_{ex} > \sigma_{pr}$ is

$$p = \frac{1}{B} \sum_{j=1}^{B} I(\sigma^j_{ex} - \sigma^j_{pr} > 0), \qquad (4)$$

where $B = 9,999$ and $I()$ is the indicator function, which is equal to 1 when its argument is true and 0 otherwise. The
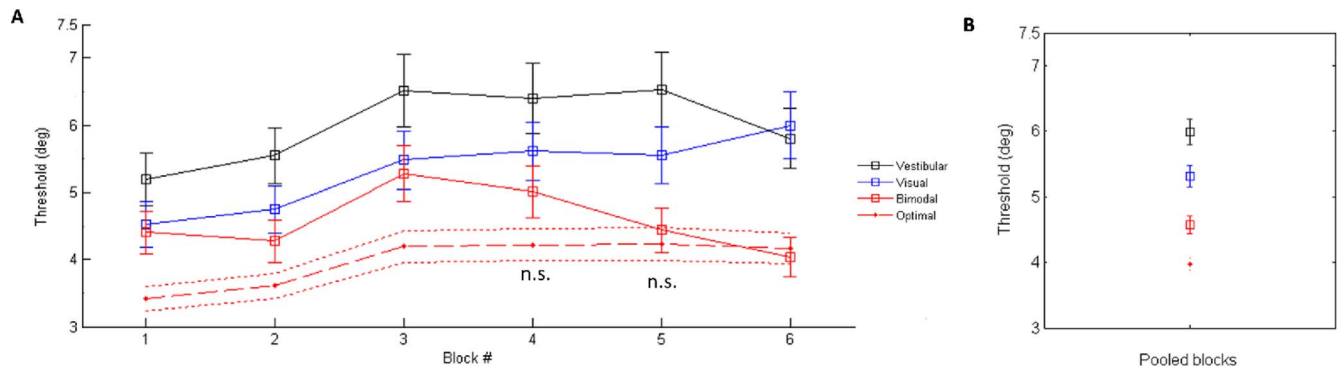
Figure 2. Experiment 1 (vestibular yaw + visual roll stimulation). (A) Integration of vestibular and visual cues in Experiment 1 is shown across the six blocks. The difference between the predicted and the experimentally measured threshold becomes nonsignificant in the last two blocks, compatible with optimal visual–vestibular integration. Blocks where the bimodal threshold is not significantly different from the predicted one (i.e., optimal integration) are marked by "n.s." ($p > 0.05$, one-tailed bootstrap test). Error bars represent bootstrap standard error. (B) The same analysis performed for data pooled across blocks and participants.

inequality would be reversed for the probability of $\sigma_{ex} < \sigma_{pr}$. The one-tailed bootstrap p value is therefore simply the proportion of values of $\sigma_{ex}^j - \sigma_{pr}^j$ that are more extreme than 0. We prefer this approach to parametric testing because it provides a direct computation of the cumulative distribution of a test statistic instead of requiring the use of an asymptotic approximation.

The threshold values obtained through the boot-strapping were also analyzed using repeated-measures ANOVAs. In the group analysis (see Results), the threshold values pooled across subjects were used in a 6 × 3 ANOVA (with six blocks and three conditions as factors). For the single-subject analysis, the ANOVAs were performed on the bootstrapped values from single subjects for each block and condition. Bonferroni post hoc comparisons were used to explore the result of the interactions.

Results

For both experiments, the same analyses were performed. We first explored the results of our subjects as a group and then conducted more detailed analyses on single-subject data.

Experiment 1. Vestibular yaw and visual roll: Group analysis.

A 6 × 3 repeated-measures AN-OVA with blocks (six) and conditions (three) as factors yielded significant main effects and interaction (all $ps < 0.0001$). All Bonferroni post hoc comparisons were significant (all $ps < 0.0001$, except for Block 5 unimodal visual threshold not being different from Block 2 unimodal vestibular threshold). Next, we performed a one-tailed bootstrap analysis collapsing all blocks for all participants, which revealed a significant

difference between the two single cues (vestibular threshold = 6.0, visual threshold = 5.3; $p = 0.004$). The bimodal threshold was significantly different from the best single cue, i.e., visual (bimodal threshold = 4.6; $p = 0.0001$), and from the threshold predicted by the OBE (predicted threshold = 3.97; $p = 0$).

We further divided the data (pooled across subjects, as described previously under Data analysis) according to the six experimental blocks that our participants performed. Figure 2 summarizes the experimentally obtained and predicted discrimination thresholds for each of the six experimental blocks. In the first four blocks, the difference between the best single-cue thresholds and the bimodal thresholds did not differ significantly (all $ps > 0.1$). Bimodal thresholds—those measured experimentally and those predicted by the OBE model—also differed significantly (one-tailed bootstrap test, $p < 0.03$), consistent with the absence of statistically optimal visual–vestibular integration. A significant difference between the best single-cue thresholds and the empirically measured bimodal thresholds emerged only in the last two blocks ($p < 0.02$), signaling integration. In these last two blocks, participants' bimodal thresholds also became not statistically different from the predicted thresholds ($p > 0.05$; Figure 2).

We next conducted a more detailed analysis of each condition separately (visual, vestibular, and visual-vestibular) over the six blocks. Table 1 contains the results of the linear regression analysis for each condition over the experimental blocks as well as the p values of the bootstrap test comparing the thresholds of the first and last blocks. For the unimodal vestibular condition, no significant changes of the discrimination thresholds were observed over time ($r^2 = 0.31$, $p = 0.25$). The same analysis for the unimodal visual condition showed a significant difference between the first and last experimental blocks ($p = 0.005$) due to a linear

Between-block comparisons for each condition in both experiments

| Condition | Linear regression | | Bootstrap *p* value |
	R^2	*p* value	Blocks 1 to 6
Experiment 1 (yaw + roll)			
vestibular	0.31	0.25	0.15
visual	0.89	**0.01**	**0.01**
bimodal	0.03	0.73	0.19
Experiment 2 (yaw + pitch)			
vestibular	0.90	**0.00**	**0.02**
visual	0.01	0.88	0.45
bimodal	0.04	0.71	0.25

Table 1. Between-block comparisons for each condition in both experiments. *Notes*: R^2 and *p* values of the linear regression and bootstrap analysis within each condition for the two experiments. Bold values represent a significant change in threshold values across blocks.

increase of the threshold values ($r^2 = 0.89$, $p = 0.005$). Finally, the bootstrap test for the bimodal condition showed that the thresholds did not significantly change between the initial and final blocks ($p = 0.19$; a linear change was not observed, $r^2 = 0.03$, $p = 0.73$). Contrary to the ANOVA, there was no significant difference between the unimodal vestibular and visual threshold values in any of the blocks (although a trend for a difference was found in Blocks 2, 3, and 5, $p = 0.06$, 0.06, and 0.07, respectively), indicating well-matched single-cue reliabilities between the two sensory modalities. This suggests that the emergence of optimal multisensory integration for incongruent but temporally co-occurring visual–vestibular stimuli is in our case revealed by a stable bimodal threshold which did not accompany a progressive increase in the visual

threshold, thereby exposing a relative reduction of perceptual variance when cues are combined.

Experiment 1. Vestibular yaw and visual roll: Single-subject analysis

We performed 6 × 3 (block × condition) repeated-measures ANOVAs on the values for each subject generated by the bootstrap procedure. Bonferroni post hoc comparisons between the bimodal and the best unimodal cue showed integration for four subjects: Subject 3 in Block 6, Subject 4 in all blocks except Block 4, Subject 5 in Block 5, and Subject 6 in all blocks except Blocks 3 and 6. To quantify the extent of overall integration for each subject, we performed a within-subject test comparing the bimodal threshold to the predicted threshold values (Figure 4; Table 2). The tests were performed by pooling all blocks together per subject in order to yield enough data points for a statistical comparison. Four subjects out of eight in Experiment 1 showed optimal integration. Out of the four remaining subjects for whom this analysis showed no optimal integration, Subject 1 showed integration in the last two blocks (optimal in Block 6), Subject 3 showed integration only in Block 6, Subject 5 only in Block 5, and Subject 8 in Blocks 4 and 6 (Figure 4). The differences between this analysis and the results of the ANOVA are due to the latter results being skewed by high threshold values in one of the conditions in one of the blocks for some subjects.

To assess intersubject variability, we analyzed the performance of individual subjects in each of the six experimental blocks (Figure 5). To quantify the extent of integration, we subtracted the bimodal threshold values (white bars) and the values predicted by the OBE model (red lines) from the best single-cue thresholds.
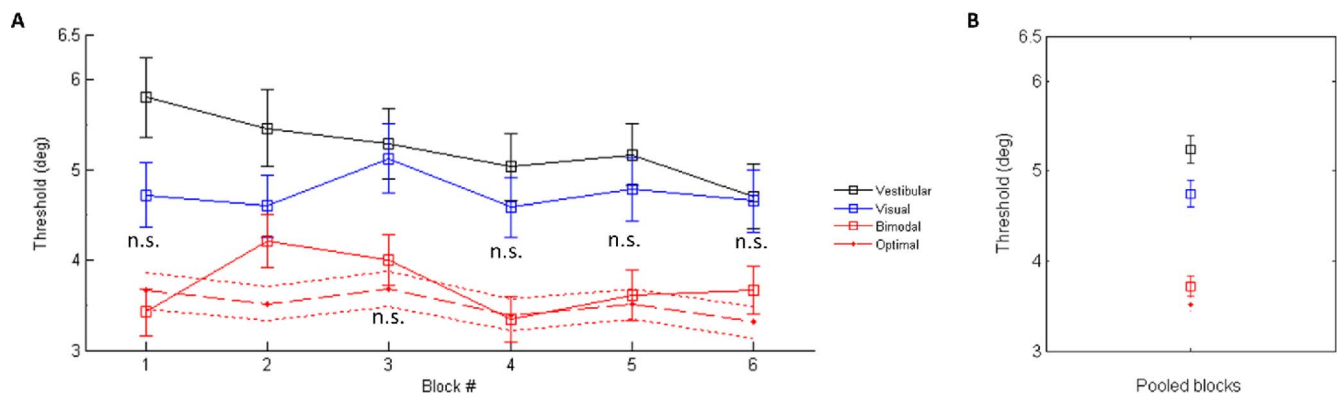

Figure 3. Experiment 2 (vestibular yaw + visual pitch). (A) Integration of vestibular and visual cues in Experiment 2 is shown across the six blocks. All blocks except Block 2 showed responses compatible with optimal visual–vestibular integration (i.e., no significant difference between the predicted and the experimentally measured threshold). Blocks where the bimodal threshold is not significantly different from the predicted one (i.e., optimal integration) are marked by "n.s." ($p > 0.05$, one-tailed bootstrap test). Error bars represent bootstrap standard error. (B) The same analysis performed for data pooled across blocks and participants.
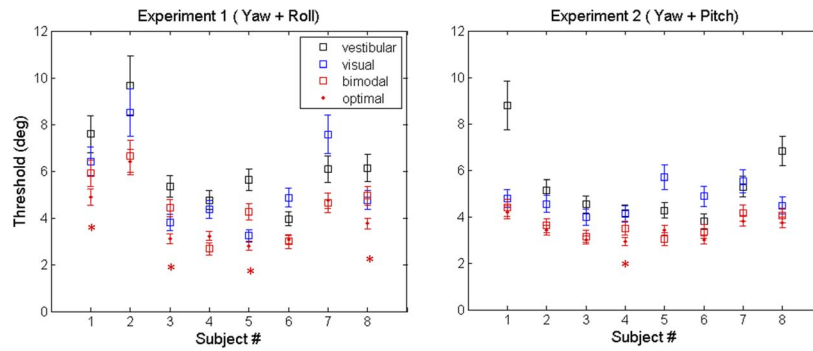
Kaliuzhna et al.

Figure 4. Individual subject data. Vestibular, visual, bimodal, and predicted thresholds for each subject for the entire experiment. A red star represents significantly higher bimodal than predicted thresholds (i.e., no optimal integration). Left panel: Experiment 1 (yaw + roll). Right panel: Experiment 2 (yaw + pitch). Error bars are bootstrap standard errors.

Positive values represent cue integration, which may or may not be optimal (this can be assessed by the proximity of the white bars and the red lines: White bars at the level of or above the red lines suggest optimality). Subject 1 is an example participant who learns to integrate the two cues only in the last two experimental blocks (negative white bars in all blocks but 5 and 6); the integration moreover seems to reach optimality in Block 6.

The results of Experiment 1 indicate that it is possible to learn to integrate visuo-vestibular cue pairings, which each signal self-motion around a different axis. In order to further corroborate this finding, we decided to use another set of stimuli that also have a high degree of disparity: vestibular yaw and visual pitch rotations.

Experiment 2. Vestibular yaw and visual pitch: Group analysis

A 6×3 repeated-measures ANOVA with blocks (six) and conditions (three) as factors yielded significant main effects and interaction (all ps < 0.0001). All Bonferroni post hoc comparisons were significant (all ps < 0.0001, except for Block 6 unimodal vestibular threshold and Block 4 unimodal visual threshold not being different from Block 2 unimodal visual threshold). Next, a general one-tailed bootstrap analysis collapsing across the experimental blocks and participants revealed the following results: There was a significant difference between the visual and vestibular thresholds (vestibular threshold = 5.2, visual threshold = 4.7; $p = 0.01$), and the bimodal threshold differed significantly from the best single cue, i.e., visual (bimodal threshold = 3.7; $p = 0$), but not from the threshold predicted by the OBE model (predicted threshold = 3.5; $p = 0.06$).

For further analysis, we divided the data (pooled across subjects, as described under Data analysis and done in Experiment 1) according to the six blocks performed. Figure 3 summarizes the experimentally obtained and predicted discrimination thresholds for each of the six experimental blocks. For the yaw–pitch combinations, participants' bimodal thresholds were not significantly different from the optimal prediction in all but the second experimental block (one-tailed bootstrap test, $p > 0.05$), and in the same blocks, the

	Experiment 1 (yaw + roll)		Experiment 2 (yaw + pitch)	
Subject	Bimodal to optimal	Bimodal to best single cue	Bimodal to optimal	Bimodal to best single cue
1	0.05	0.27	0.34	0.22
2	**0.39**	**0.05**	**0.27**	**0.02**
3	0.00	0.11	**0.31**	**0.03**
4	**0.05**	**0.00**	0.04	0.09
5	0.00	0.01	**0.14**	**0.00**
6	**0.39**	**0.01**	0.15	0.15
7	**0.44**	**0.02**	**0.21**	**0.02**
8	0.00	0.37	0.20	0.19

Table 2. Single-subject analysis. *P* values of the bootstrap comparison. *Notes*: *P* values of the one-tailed bootstrap analysis testing whether the bimodal thresholds are greater than the theoretically predicted values and whether the bimodal thresholds are lower than the best single cue for each subjects for all experimental blocks pooled together. Numbers in bold indicate the subjects who integrated (optimally).
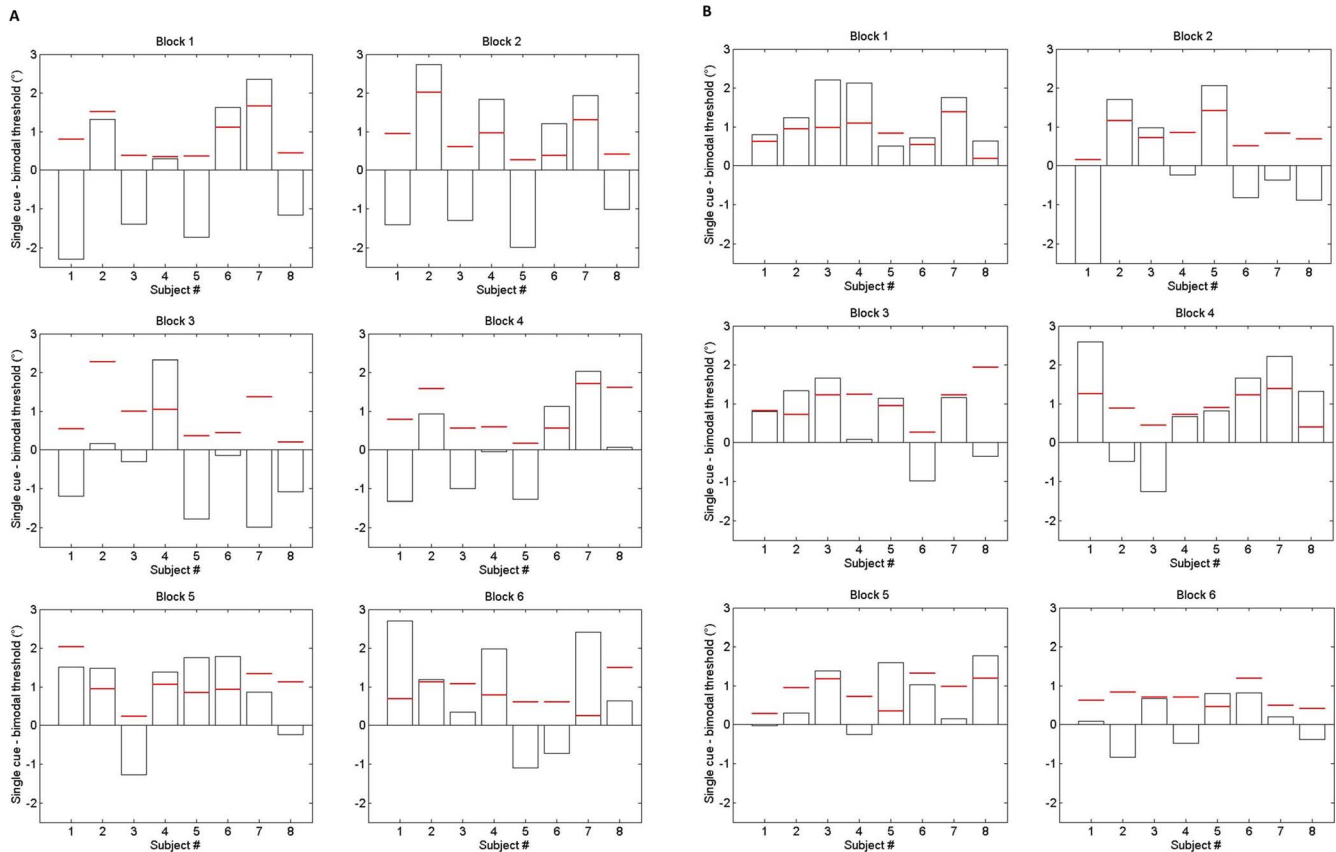
Figure 5. Individual subject data. Difference between the lowest single-cue standard deviation and the measured (white bars) and predicted (red lines) bimodal standard deviations across the six experimental blocks. Positive values indicate integration. (A) Experiment 1 (yaw + roll). (B) Experiment 2 (yaw + pitch).

experimentally measured bimodal thresholds were significantly lower than the best single-cue estimates ($p < 0.05$). In the case of yaw–pitch pairings, subjects therefore optimally integrated the two incongruent cues from the onset and throughout the tested experimental blocks (except Block 2).

As for Experiment 1, we performed a detailed analysis of the discrimination thresholds in each condition over the six blocks. The regression and the bootstrap test results are summarized in Table 1. For the unimodal vestibular condition, a significant difference was observed between the first and last experimental blocks ($p = 0.022$) due to a linear decrease of the threshold values ($r^2 = 0.9$, $p = 0.004$). For the unimodal visual condition, there was no change in the discrimination thresholds over time ($r^2 = 0.006$, $p = 0.88$). There was a significant difference between the two unimodal conditions, but only in the first two experimental blocks, once again indicating well-matched single-cue discrimination thresholds. In the bimodal condition, the threshold values showed no overall linear change ($r^2 = 0.04$, $p = 0.7$) and no significant difference between the start and end of the experimental session ($p = 0.25$).

Experiment 2. Vestibular yaw and visual pitch: Single-subject analysis

With 6×3 (block $\times$ condition) repeated-measures ANOVAs on the values for each subject generated by the bootstrap procedure and subsequent Bonferroni post hoc comparisons between the bimodal and the best unimodal cue, we found integration for five subjects: Subject 2 in all blocks but 4 and 6; Subject 3 in all blocks but Block 4; Subject 4 in Blocks 1, 3, and 4; Subject 5 in all blocks but 1 and 4; and Subject 6 in all blocks but 2 and 3. The results of single-subject bootstrap analysis from Experiment 2 are shown in Figures 4 and 5 (see also Table 2). This analysis revealed that seven out of eight subjects in Experiment 2 showed optimal integration. The difference between the bootstrap test and the ANOVA is again due to high variance in one block and condition skewing the results of the ANOVA. An example of a participant who integrates throughout Experiment 2 is Subject 5 (white bars have a positive value in each experimental block), and this integration is optimal (red lines at the level of or overlapping with the white bars). This is different from Subject 4, whose bimodal thresholds are only

Kaliuzhna et al.

lower than the best unimodal thresholds in half of the blocks (Blocks 1, 3, and 4) and whose integration is optimal only in Blocks 1 and 4.

Discussion

The main finding of the present study is that human observers can optimally integrate or learn to integrate co-occurring multisensory self-motion stimuli when those stimuli imply rotations around different axes. In two experiments, we showed that participants' performance was better for directionally conflicting bimodal visuo-vestibular cues than for either vestibular or visual cues alone. In the yaw–roll experiment (Experiment 1), such optimal integration improved over successive blocks, whereas in the yaw–pitch experiment (Experiment 2) it was observed in all but one experimental block. These results extend the previous literature on self-motion perception, demonstrating that optimal integration also occurs for stimuli with large, consciously detectable discrepancies.

It has been proposed that sensory integration would only occur for stimuli attributed to the same causal event (Körding et al., 2007; Parise et al., 2012; Shams & Beierholm 2010). The present results would mean that in the bimodal condition, instead of experiencing two distinct rotational stimuli as provided by the incongruent visual and vestibular modalities, subjects perceive one single self-displacement, possibly going in an intermediate direction with respect to the two cues. Compatible with such a proposal are data from previous studies showing that selected visuo-vestibular conflicts are perceived as one single motion (Ishida, Fushiki, Nishida, & Watanabe, 2008; Wright, DiZio, & Lackner, 2005). Thus, incongruent visual and vestibular cues along the same yaw axis but indicating yaw rotations in the same direction (an ecological conflict— e.g., clockwise vestibular yaw and clockwise visual yaw) are perceived as rotations that depend more strongly on the direction of the visual stimulus, compatible with visual dominance. Findings with the vestibular-ocular reflex (VOR) are also compatible with such visual dominance. The VOR occurs when the head moves or when vection is perceived, and keeps the image stable on the retina by moving the eyes in the opposite direction. Ishida et al. (2008) found that the direction of the VOR in cases of nonecological visual-vestibular stimulus combinations in the yaw axis also reveals such visual dominance and is congruent with the visual stimulus. Also of relevance are VOR studies of cross-modal adaptation between visual and vestibular cues (indicating motion in different directions) that have been performed in several species (Baker, Wickland, & Peterson, 1987; Schultheis & Robinson, 1981; Trillen-

berg, Shelhamer, Roberts, & Zee, 2003). Subjects were exposed for a certain period of time to simultaneously presented conflicting stimuli (different axes from those employed in the present study), and adaptation was reflected in the change of the direction and gain of the VOR. These studies indicate that a visuo-vestibular conflict, in certain conditions, is formulated by the nervous system into one single percept (i.e., conscious perception of self-motion in one particular direction).

Based on our own finding of optimal integration in Experiments 1 and 2 and these previous findings, we argue that in the incongruent visual–vestibular combinations (bimodal conditions), subjects might perceive a single self-displacement. Unfortunately, no subjective reports of the perceived direction of motion have been collected in the present study or in the previous literature. In our study, only one subject (in Experiment 2) spontaneously reported a single illusory diagonal displacement during the bimodal (yaw + pitch) condition. We propose that future work could extend the present paradigms and additionally record eye movements in order to investigate whether the two conflicting motion directions are combined into a single representation and whether the resulting integrated percept depends more on the vestibular or the visual cue (as reported in related work by Ishida et al., 2008). Although the direction of perceived motion might be inferred from the direction of fixating microsaccades, the use of a stereoscopic visual stimulus necessitating shutter glasses prevented us from recording eye movements by means of video tracking. In previous studies (Ishida et al., 2008; Trillenberg et al., 2003), subjects were exposed to the same continuous stimulation for a prolonged amount of time (one to several hours) before the adaptation could be objectified with the eye-movement recording. The present findings, however, suggest that such motion integration for incompatible directions may occur much faster than previously thought.

The observed visual–vestibular integration may also depend on the demands of the experimental task and the particular stimuli chosen. Thus, multisensory integration in our study could have occurred as a result of the specific task demands, which may have made the directional conflict irrelevant to the task. Thus, in previous experiments on multisensory conflicts (including visual–vestibular stimulation but also other multisensory stimulus combinations), the response of the subject (e.g., localizing a stimulus, judging the number of stimuli, judging perceptual qualities of stimuli) was found to depend on the amount of conflict between the two stimuli. For instance, in a task where subjects are asked to localize a visual stimulus in the presence of an auditory cue from a conflicting location, perceptual unification breaks down and the two modalities bias each other less when the distance between the visual and

the auditory cues is too large (e.g., Roach et al., 2006; Wallace et al., 2004). In the present study, however, the direction of motion was irrelevant to the task we asked our participants to perform, because estimating rotation size is independent of rotation direction. As the amount of rotation provided by the visual and the vestibular cues was always the same in the present bimodal conditions, one could expect that the extraction of this feature alone could lead to the observed visual–vestibular patterns of integration. This extraction could further have been facilitated by the fact that other stimulus features were matched for the visual and vestibular stimuli despite their directional conflict. Thus the motion onset, the duration, and the spatiotemporal motion profile of both stimuli were matched. In the same vein, a recently published work reports, for instance, that simultaneous visuo-vestibular stimuli indicating the same heading direction but having a different acceleration profile are optimally integrated (Butler, Campos, & Bülthoff, 2014). Another unpublished work reports that stimuli designating the same amount of motion and having the same motion profiles (but being temporally offset) can also be learned to be integrated (Campos et al., 2009). These data indicate that, despite the fact that some properties of the two stimuli are not matched, integration occurs when the task-relevant features of these stimuli are not in conflict (i.e., most features of the stimuli are correlated). Further work is needed to disentangle the different contributions of stimulus attributes and task demands for the integration process.

Our results show that integration in the bimodal condition occurred from the beginning in Experiment 2 (vestibular yaw + visual pitch), whereas such integration only appeared during the later phases of Experiment 1 (vestibular yaw + visual roll). That is, integration of pitch with yaw was present throughout the experiment, whereas integration of roll with yaw was learned over time. To our knowledge, there exists no anatomical or functional evidence for a facilitated integration of pitch with yaw versus roll with yaw stimuli. Neither at the level of the vestibular nuclei (Büttner-Ennever, 1992; Highstein & Holstein, 2006; Naito, Newman, Lee, Beykirch, & Honrubia, 1995) nor in the cortex (Arnoldussen, Goossens, & van den Berg, 2013) can the pattern of projections from the semicircular canals account for our findings. Although recordings of neural responses to vertical rotations reveal that roll neurons outnumber pitch neurons in the brain stem (Baker, Goldberg, Hermann, & Peterson, 1984; Bolton et al., 1992; Endo, Thomson, Wilson, Yamaguchi, & Yates, 1995; Kasper, Schor, & Wilson, 1988; Wilson, Yamagata, Yates, Schor, & Nonaka, 1990), optimal activations of cortical vestibular neurons are uniformly distributed over all possible rotation planes (Akbarian et al., 1988; Grüsser, Pause, & Schreiter, 1990). Other studies looking at conflicting visuo-vestibular stimuli (e.g., Bockisch, Straumann, & Haslwanter, 2003; Waespe & Henn, 1978) have failed to provide the comparisons relevant to our study and findings (different stimulation axes and parameters of stimulation).

We do not think that our results can be attributed to the fact that participants performed in general better in Experiment 2 (lower thresholds for the unimodal conditions). Nor could this result be attributed to the fact that three subjects participated in both experiments (i.e., learned integration from Experiment 1 influenced thresholds in Experiment 2): Their performance was comparable in both experiments, and all three subjects showed integration in the majority of experimental blocks in both experiments. Accordingly, we propose that the difference between yaw–roll and yaw–pitch integration may be caused by supravestibular directional influences that have been observed previously in cognitive neuroscience. In Experiment 1, vestibular clockwise (i.e., rightward) yaw was always paired with visual leftward roll, and in Experiment 2, vestibular rightward yaw was always paired with upward pitch. Previous research on spatial compatibility (e.g., Simon effect, spatial Stroop, mental number line) has shown a facilitation effect for stimuli occurring in the same spatial plane (e.g., right + right) and for left–down/right–up pairings (Cho & Proctor, 2003; Nicoletti & Umiltà, 1984; Nishimura & Yokosawa, 2006). For instance, participants are faster to respond to visual stimuli presented on the left or at the bottom of the screen with their left hand and to rightward and upward stimuli with their right hand (for a review, see Proctor & Cho, 2006). Similarly, if vocal responses "right" and "left" are attributed to stimuli presented above or below the midline of the screen, such a random pairing yields faster responses than pairing "right" with below and "left" with above (Weeks & Proctor, 1990).

Such compatibility effects have also been shown for multisensory stimuli. For example, a high-frequency tone and a tactile stimulus at a higher location presented together (and a low-frequency tone plus a tactile stimulus at a lower location) are more strongly associated than, e.g., a high-frequency tone with a tactile stimulus at a lower location (Occelli, Spence, & Zampini, 2009). Such cross-modal mechanisms have also been shown for the vestibular system: Active head turns (Loetscher, Schwarz, Schubiger, & Brugger, 2008) as well as passive displacements (Hartmann, Grabherr, & Mast, 2012) to the right and left have been found to influence numerical cognition in a magnitude-specific way. Leftward movements facilitate the generation of smaller numbers and rightward motion that of larger numbers. A related supravestibular directional mechanism could have influenced responses in the present two experiments, meaning that processing the association of

Kaliuzhna et al.

the bimodal stimuli we have chosen is a priori facilitated due to the correspondence of spatial representations or dimensional overlap of their directions (Kornblum, Hasbroucq, & Osman, 1990; Kosslyn & Kosslyn, 1996; Li, Nan, Wang, & Liu, 2014). Given the strong implication of vestibular signals for space perception, the existence of such automatic associations seems highly plausible. Indeed, the pairing of visual (simulated) rightward roll with rightward vestibular yaw and rightward vestibular yaw with upward pitch might represent a preferred direction for integration, potentially providing a partial explanation for our results.

Alternatively, other characteristics shared between yaw and pitch stimuli might contribute to the faster integration observed in Experiment 2. For instance the gain of the VOR elicited by both yaw and pitch movement or optic flow is generally close to 1.0, whereas the gain of the torsional VOR elicited by roll movement is generally more limited (Tweed et al., 1994). The optic flow resulting from yaw and pitch movements involves the motion of the whole visual field in one direction, whereas in the roll plane the visual scene rotates around a central point (Duffy & Wurtz, 1995). Finally, it may be that in daily life, combined yaw–pitch head motion (i.e., up and to the right) is more frequent than combined yaw–roll motion, although this speculation has yet to be confirmed by empirical research. These natural constraints may separately or in combination with the mentioned supravestibular mechanism result in a multisensory system that is more tolerant to conflicts between stimuli sharing a larger number of common characteristics.

Although of no direct relevance for the integration results we report, it should be noted that the fluctuations of unimodal thresholds were not the same in the two experiments. During Experiment 1, the unimodal visual threshold became progressively more elevated over consecutive sessions, which was not observed in Experiment 2. We speculate that this change can be attributed to fatigue or decreased attention over time as the subjects took part in a prolonged experiment requiring a continued high level of visual attention. In Experiment 2, however, the vestibular threshold was reduced over time. We presume that this reduction can be attributed to perceptual learning or improvement as subjects repeatedly experience the same stimulus. It is safe to assume that these idiosyncratic phenomena are also present and affect perception in the same way when the unimodal stimuli are paired with one another in the bimodal condition. The increasing visual thresholds in Experiment 1 and the decreasing vestibular thresholds in Experiment 2 therefore impact the bimodal prediction as well. Despite these changes,

the experimental bimodal threshold still closely matched this prediction, thus showing optimal integration.

Finally, our result may be of relevance for visual–vestibular integration in neurological patients. It has been suggested that illusory own-body perceptions such as room-tilt illusions, inversion illusions, and out-of-body experiences are related to abnormal multisensory integration involving the visual and the vestibular senses (Blanke, 2012; Ionta et al., 2011; Lopez, Halje, & Blanke, 2008). Our experiments show that conflicting information from these two modalities is optimally integrated by the brain, possibly to produce a single percept and thus merge contradictory visual and vestibular self-motion cues into one coherent representation. We argue that such a single representation may also account for illusory own-body perceptions related to self-location and self-motion during such neurological conditions. Abnormal perception in these illusory states could be due to a statistically optimal integration of abnormal visuo-vestibular cue pairings instead of, as often claimed, a failure to integrate multisensory cues which may be providing conflicting information about self-motion and self-location. Neurological patients with out-of-body experiences caused by cortical damage (Ionta et al., 2011) and healthy subjects who are prone to out-of-body experiences (e.g., Murray & Fox, 2005) may integrate visual and vestibular stimuli across a larger range of stimulus incompatibilities than subjects without such experiences. This interpretation, however, is to be taken with caution, as it is yet to be supported by experimental evidence and the illusory own-body perceptions are related to abnormal processing of gravitational information (i.e., depend on the otolith organs), whereas our experimental manipulations involved vestibular yaw rotations and only partly involved visual gravitational stimulation.

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Kaliuzhna et al.

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Study 2: Optimal visuo-vestibular integration for self-motion perception in patients with unilateral vestibular loss

Personal contribution: performed research, wrote the paper.

Optimal visuo-vestibular integration for self-motion perception in patients with unilateral vestibular loss

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Abstract

Objectives: Patients with unilateral vestibular loss (UVL) suffer from an impairment of several vestibular-mediated functions and were previously reported to present with faulty multisensory interactions. Visuo-vestibular integration for the perception of self-motion has not been formally tested in UVL patients although it might play an important role in their vestibular compensation. For the first time we investigated the presence and optimality of visuo-vestibular integration in UVL patients.

Methods: Patients were seated on a rotating platform with a screen simulating 3D rotation in front of them. They had to judge the relative magnitude of two successive rotations in three conditions: vestibular alone (chair rotation), visual alone (simulated rotation) and bimodal (both stimuli together). Healthy subjects exhibit better performance on this task in the bimodal condition, and their performance is statistically optimal according to the optimal Bayesian estimator model (OBE) employed here.

Results: Patients exhibited optimal multisensory integration during both ipsi- and contralesional rotations. The benefit of multisensory integration was more pronounced on the impaired side.

Conclusions: Intact optimal multisensory integration is present in patients with unilateral vestibular loss, despite absent information form one labyrinth, and might be the basis of functional recovery in this condition.

Introduction

Healthy subjects base their judgements about self-motion on an optimally integrated percept of visual and vestibular cues, in order to reduce the perceptual uncertainty associated with each cue [4, 12]. Whether the same is true when one of these modalities is impaired was investigated here in patients with unilateral vestibular loss (UVL) during passive whole-body rotations.

In healthy subjects yaw rotation is encoded by the activation of vestibular afferents from the ipsilateral horizontal semi-circular canal and the simultaneous inactivation of vestibular afferents from its contralateral homologue[6]. In the case of complete unilateral vestibular loss, no information about rotation from the vestibular system is available from one side, reducing the information available for encoding self-motion. UVL patients have a decreased ability to discriminate the direction of passive whole-body rotations, a deficit thought to be subtended by increased neuronal detection thresholds for self-motion in vestibular nuclei neurons[7]. Furthermore, after UVL the rotational vestibular-ocular reflex (VOR) is asymmetrical during passive vestibular stimulation [1, 2], the gain of optokinetic nystagmus is decreased, and there is cortical suppression for the processing of visual motion[2]. Interestingly, previous research also points to abnormal multisensory integration in patients with unilateral vestibular loss; difficulties in integrating visual, vestibular and proprioceptive information have been described for postural control and spatial navigation[10, 14].

Whether similar deficits are observed for multisensory integration during the perception of passive self-motion has not to our knowledge been directly tested in UVL patients within a quantitative theoretical framework. Using previously reported experimental setup and paradigm [12] we explored the limits of visuo-vestibular integration in a cohort of UVL patients. Patients were exposed to three types of passive whole-body rotations in the yaw plane. In the unimodal conditions, rotations were either provided by a rotating platform or simulated by visual optic flow. The bimodal stimulus was a combination of the two cues occurring simultaneously in congruent directions. Patients were asked to judge the relative size of two successive rotations of the same type. One was the standard rotation of fixed size and the other's size was varied from trial to trial. Psychometric functions were fit to the patient's estimates and perceptual thresholds extracted from the fits. Visuo-vestibular integration would result in bimodal perceptual thresholds being lower than for the unimodal conditions. Such integration is considered optimal if the empirically obtained bimodal threshold does not differ from the predictions of an optimal Bayesian estimator (OBE).

Participants

Eight patients with unilateral peripheral vestibular loss (mean age=42.25, 22-57yrs, 3 women) participated in the study (Table 1). Complete unilateral peripheral vestibular loss was shown by a pathologic Head Impulse Test (absence of VOR for high frequency rotations) and caloric areflexia on the lesion side (absence of VOR for low frequency rotations). A local ethics committee approved the study and all patients signed an informed consent form in accordance with the Declaration of Helsinki.

Table 1. Patients' clinical data

Patient	Age (years)	Gender	Post-operative time (months)	Diagnosis	Lesion side
1	23	m	9	transverse temporal bone fracture	R
2	58	f	9	labyrinthectomy (Menière's)	L
3	57	m	4	idiopathic vestibular deficit	L
4	54	m	261	vestibular neurectomy (Menière's)	R
5	46	f	<60	vestibular schwannoma	L
6	37	m	15	transverse temporal bone fracture	R
7	35	m	62	vestibular schwannoma	L
8	36	f	20	vestibular schwannoma	R

Materials and Methods

Optimal Bayesian Estimator

For a given whole-body rotation of size *S* the visual and the vestibular modalities each provide an independent estimate of S with a certain degree of perceptual uncertainty, which can be measured as their trial-by-trial variance σ_{vi}^2 and σ_{ve}^2, respectively. Maximum likelihood estimation (derived from Bayes' rule) dictates that if the two unimodal cues are integrated according to statistical optimality, the uncertainty associated with the bimodal estimate σ_{bi}^2 is reduced relative to the unimodal uncertainties according to:

$$\sigma_{bi}^2 = \frac{\sigma_{vi}^2 \sigma_{ve}^2}{\sigma_{vi}^2 + \sigma_{ve}^2} \qquad (1)$$

Experimental Setup

As described previously[8, 12] participants were seated in a rotating chair and were comfortably restrained using a five-point racing harness, foot-straps and additional cushioning. A chin-rest and head-fixation were used to prevent head motion.

The rotation chair was digitally servo-controlled (PCI-7352), had precise positioning of around 0.1° and was centred on the rotation axis. The chair delivered the vestibular stimuli in the form of yaw-plane rotations. The rotation profiles of the chair were pre-set and designated the immediate angular position of the chair at a rate of 100 Hz. The velocity profile *v(t)* of the rotations was a single cycle of 0.77 – Hz raised cosine function

$$v(t) = \frac{A}{T}\left[1 - \cos\left(\frac{2\pi t}{T}\right)\right] \qquad (2)$$

where *A* is rotation size and *T* is its duration (*T* = 1.3 s in this case). Instantaneous angular position *p*(*t*) is then specified as

$$p(t) = A\left[\frac{t}{T} - \frac{1}{2\pi}\sin\left(\frac{2\pi t}{T}\right)\right] \qquad (3)$$

A 22 inch display was fixed to the chair at a distance of 29 cm in front of the patients for delivering the visual stimulus. The limited visual field covered ∼80° of horizontal and 56° of vertical visual angle. The visual image consisted of a stereoscopic pattern of randomly distributed moving dots of different size. The dots were two dimensional symmetric greyscale Gaussian blobs with a minimum and maximum standard deviation of 0.5 and 3 pixels respectively. Rotation was simulated by placing the subject's view-point in the middle of the scene and rotating it around the yaw axis. A stationary point (filled red circle with a radius of 3 pixels, 0.5 intensity level presented at zero binocular disparity) was displayed in the centre of the screen in all conditions during rotation and the patients were instructed to fixate it. The stereoscopic visual stimulus was generated by the Nvidia Quadro FX 3800 graphics card using the OpenGL quad-buffer mechanism. The stimulus was programmed with the Python language and viewed with the Nvidia 3D Vision kit (active shutter glasses) paired with a Samsung Syncmaster 2233RZ display (120-Hz refresh rate) via an infrared transmitter. The velocity

and onset of the optic flow was the same as of the rotating chair. Masking white noise was presented over headphones throughout the task.

Experimental Paradigm

On each trial two successive rotations in the same direction were presented (the standard and the test). In an alternative forced-choice task patients had to judge their relative size. There were three types of trials: vestibular alone (rotations delivered by the chair alone, the screen was black, displaying only the fixation point), visual alone (rotation of the visual optic flow with the chair stationary), and a bimodal condition where both rotations occurred simultaneously and in congruent (i.e. opposite) directions. The size of the standard rotation was 15°, and the test rotation was any of 7 equally spaced angles in the interval 10°-20° tested using the method of constant stimuli. The two rotations were preceded, followed, and separated by an interval of 0.5 s. The patients then had 2 seconds to answer, via a button press, whether the second rotation was bigger or smaller than the first. The standard rotation was randomly presented as either the first or second stimuli.

Based on our previous experiments we used a 50% level of visual coherence (number of dots simulating rotation/number of dots moving randomly), which was shown to produce visual perceptual thresholds matched with the vestibular thresholds in healthy subjects [12].

At the beginning of the experiment the patients performed a short (10 trials) training session that was repeated until a correct response was obtained for the majority of trials (usually 3 to 4 repetitions). The experiment then began and lasted for about 1 h and 30 min. The experiment was divided into sessions of approximately 5 minutes that were grouped into 6 blocks. This was done in order to ensure that the patients will get a sufficient amount of rest when they required it. Every session contained trials of each of the three conditions presented in a randomised order, making it impossible to predict which condition would occur next. Patients performed a total of 420 trials divided evenly over 6 blocks. The direction of rotation was randomly chosen on each trial. There were an equal amount of clockwise and counter clockwise rotations.

Data Analysis

All data analyses were performed off-line with custom programs compiled in MATLAB (The MathWorks). For each test angle, individual answers were pooled across all patients (or, for individual patient results – across experimental blocks) to obtain a probabilistic measure of the response and yield a sufficient sample set for the statistical comparisons. This consisted of calculating

the proportion of "bigger" responses and fitting them with a cumulative Gaussian function. Measures of the mean, the variance, and of the discrimination threshold were then extracted from the obtained fits in each condition. A bootstrap analysis provided standard errors for each measure and allowed statistical comparison between the experimentally measured values and model predictions. This consisted of repeating the data fit for each condition 9999 times on a different subset of responses each time. The different subsets were formed by taking at random, with replacement, *N* trials from the total set of *N* for each test angle. The standard deviation of 9999 repeated measures is then the standard error of the measure obtained using the original data set. Statistical tests were made by assessing the amount of overlap between the bootstrap iterations of two measures. If the measure of interest is σ, and σ_{ex}^{j} and σ_{pr}^{j} are its experimental and predicted estimates obtained from the *j*th bootstrap sample, then the bootstrap probability of ($\sigma_{ex} > \sigma_{pr}$) is

$$ p = \frac{1}{B} \sum_{j=1}^{B} I\left(\sigma_{ex}^{j} - \sigma_{pr}^{j} > 0\right), $$

where *B* = 9999 and *I*() is the indicator function, which is equal to 1 when its argument is true and 0 otherwise. The inequality would be reversed for the probability of ($\sigma_{ex} < \sigma_{pr}$). The one-tailed bootstrap *P* value is therefore simply the proportion of ($\sigma_{ex}^{j} - \sigma_{pr}^{j}$) values that are more extreme than 0. We prefer this approach to parametric testing because it provides a direct computation of the cumulative distribution of a test statistic instead of having to use an asymptotic approximation. For the analysis we divided the data for each patient according to whether the rotation was performed in the direction of the vestibular lesioned or non-lesioned side .

Results

We pooled trials across all blocks and all patients in order to test for visuo-vestibular integration on the healthy versus the deficit side (Figure 1). For stimuli towards the healthy side, statistical analysis (bootstrap test) revealed that the empirical bimodal threshold did not differ significantly from the vestibular alone (best single cue) threshold (p=0.07); and the empirical bimodal threshold did not differ significantly from the predicted threshold (p=0.41). On the deficit side, the bimodal threshold was significantly lower than the vestibular alone threshold (p=0.0013), and not significantly different (p=0.08) from the threshold predicted by the OBE, indicating that the patients performance was improved by having access to both cues. There was a significant difference between the two single cues on both sides (visual, p=0, and vestibular, p=0.0029). Neither the visual nor the vestibular or the

bimodal thresholds changed significantly between the healthy and the deficit sides (visual cue, p=0.42; vestibular cue, p= 0.11; bimodal, p=0.43).
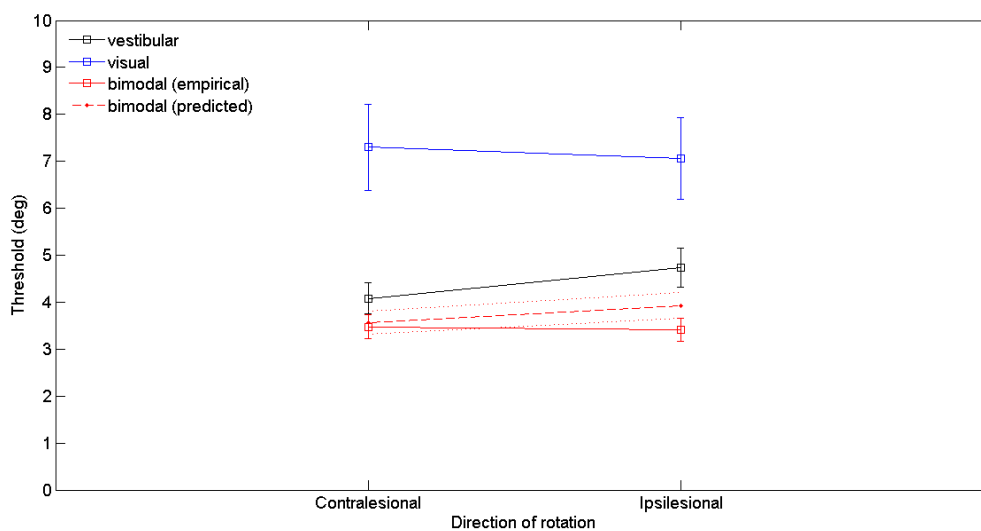

Figure 1. Integration of visual and vestibular cues after ipsilesional (deficit side) and contralesional (healthy side) rotations. On the healthy side, integration was optimal but the bimodal threshold was not significantly lower than the vestibular alone threshold. On the deficit side integration was optimal and the bimodal threshold was significantly lower than the vestibular alone threshold. Error bars represent bootstrap standard error.
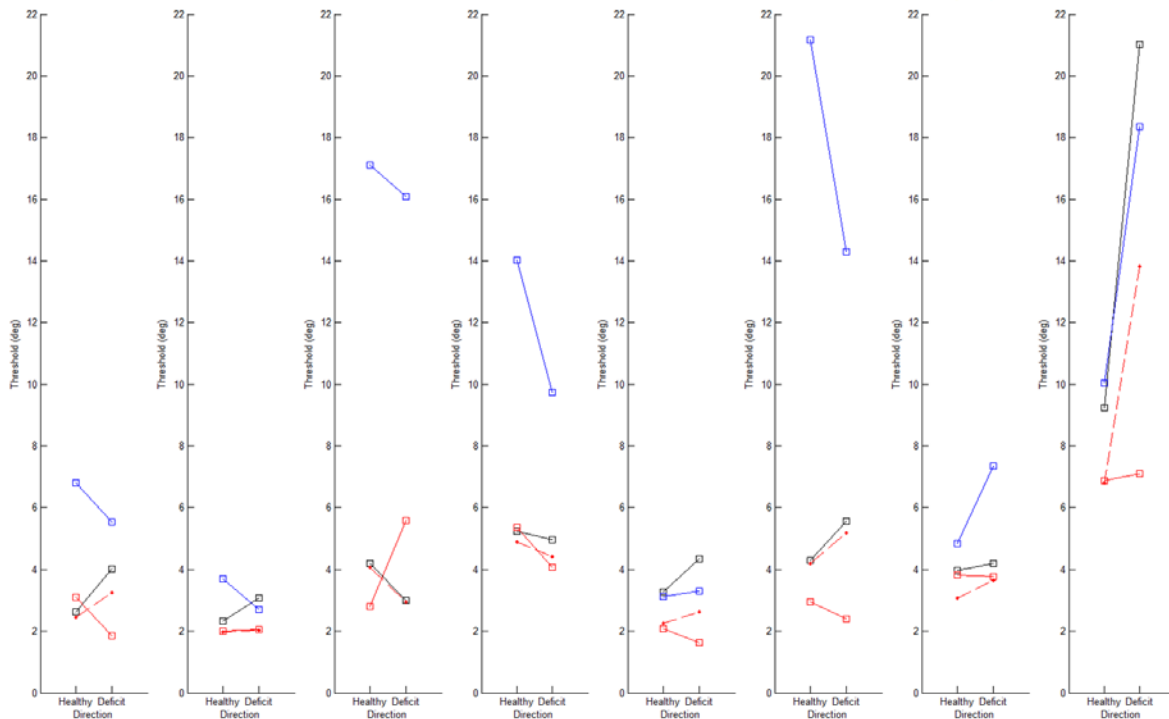
Figure 2. Individual patient results.

Discussion

Multisensory integration would appear a crucial compensatory mechanism for the estimation of self-motion in the presence of unilateral vestibular loss. When repetitively estimating the amount of a passively executed rotation, each sensory modality is affected by a certain level of neural (peripheral and central processing) and physical (characteristics of the stimulus itself) noise, resulting in judgement variability, which is further increased in UVL patients. Our study sought to investigate the presence, amount and optimality of multisensory integration in such conditions. We demonstrated that UVL patients have a more pronounced benefit from optimal multisensory visuo-vestibular integration during ipsilesional rotations.

The bimodal thresholds in our patients were not significantly different form the thresholds predicted by the OBE, implying optimal multisensory integration. We suggest that this integration in patients occurs due to the interleaved functional and anatomical processing of visual and vestibular information. Under ecological conditions visual and vestibular cues occur simultaneously and are highly correlated, providing complementary information about the nature of self-motion, with the visual system being more sensitive to low-frequency, low-amplitude motion and vice versa for the vestibular system[11]. Congruent visual and vestibular self-rotation cues are fused at the perceptual

level, whereby unisensory information is discarded and only the combined percept is accessible to the subject [12]. Conflicting visuo-vestibular cues are also integrated in a statistically optimal fashion[8]. In terms of anatomy, bimodal neurons responding to both passive self-rotation/translation and optokinetic stimulation are found at the first stage of vestibular processing in the vestibular nuclei. In primates, several cortical areas host bimodal visuo-vestibular neurons[9]. Despite abnormal sub-cortical processing compared to healthy subjects, information from only one semi-circular canal in UVL patients appears to be sufficient for accurate perceptual judgements.

Visuo-vestibular integration appeared enhanced in our patients during ipsilesional rotation trials. During such rotations only an inactivated signal from the healthy labyrinth provides information about the vestibular stimulus. We explain this result in terms of a previously described multisensory mechanism of inverse effectiveness [3, 13]. At the neural level, the multisensory response of a neuron is enhanced when the unisensory inputs only weakly activate it. Several studies have shown the benefits of inverse effectiveness for behavioural performance in patient populations. In patients with hemianopsia and visuo-spatial neglect, detection of a visual target as well as visual attention are improved when a simultaneous auditory stimulus is presented in the same spatial location, as compared to no auditory stimulus. This effect was most pronounced in the affected hemifield; the lower the unisensory detection rate, the greater the multisensory enhancement reported[5, 15]. These results are interpreted in light of multisensory visuo-auditory neurons extensively described in the superior colliculus, which robustly enhance multisensory responses in the presence of weak unisensory stimuli. A similar mechanism might explain the results in our patients, pointing towards a unique set of multisensory integration principles over neurons coding for different sensory modalities in different brain areas.

Visual thresholds were higher than vestibular thresholds in the tested patients (Figure 2). The level of visual motion coherence used for the visual stimulus was previously found to best match the difficulty of the vestibular cue in a cohort of healthy young participants [12], but appeared to be too low for the patients. Previous studies have shown that UVL patients manifest decreased sensitivity to visual motion accompanied by diminished cortical activity in the visual cortex (possibly as a mechanism to reduce oscillopsia) [2] as well as other difficulties in processing visual information [14]. Remarkably, despite the elevated visual threshold, we still observed optimal multisensory integration in the patients.

In conclusion, our study for the first time provides evidence for optimal multisensory integration of visual and vestibular cues in patients with unilateral vestibular loss. This intact mechanism together

with other compensatory processes, such as reliance on proprioceptive and visual information, could underlie the behavioural recovery in this condition.

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Part 2. Vestibular-tactile & visuo-vestibular tactile interactions

Study 3: Vestibular-somatosensory interactions: effects of passive whole-body rotation on somatosensory detection.

Personal contribution: designed research, performed research, wrote the paper.

PLOS ONE

Vestibular-Somatosensory Interactions: Effects of Passive Whole-Body Rotation on Somatosensory Detection

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Abstract

Vestibular signals are strongly integrated with information from several other sensory modalities. For example, vestibular stimulation was reported to improve tactile detection. However, this improvement could reflect either a multimodal interaction or an *indirect* interaction driven by vestibular effects on spatial attention and orienting. Here we investigate whether natural vestibular activation induced by passive whole-body rotation influences tactile detection. In particular, we assessed the ability to detect faint tactile stimuli to the fingertips of the left and right hand during spatially congruent or incongruent rotations. We found that passive whole-body rotations significantly enhanced sensitivity to faint shocks, without affecting response bias. Critically, this enhancement of somatosensory sensitivity did not depend on the spatial congruency between the direction of rotation and the hand stimulated. Thus, our results support a multimodal interaction, likely in brain areas receiving both vestibular and somatosensory signals.

Competing Interests: The authors have declared that no competing interests exist.

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Introduction

Vestibular signals contribute to several complex behaviours and cognitive functions and are integrated with inputs from other sensory modalities. For example, the vestibular system plays a key role in spatial orientation and self-motion detection. Consistent with this view, functional neuroimaging studies in humans revealed that vestibular inputs project to a network of subcortical and cortical multimodal areas, particularly to the posterior insula and adjacent operculum [1,2,3,4,5].

Critically, the vestibular cortical projections strongly overlap with the somatosensory cortical projections [4,5,6,7]. There is growing evidence for multisensory perceptual interactions between vestibular and somatosensory signals. Both caloric and galvanic vestibular stimulation (CVS, GVS respectively) were shown to modulate tactile perceptual thresholds [8,9], and somatosensory-evoked potentials (SEPs) [10]. In particular, CVS selectively enhanced the N80 SEPs wave [10], whose source has been localised in the parietal operculum [11,12]. Clinical studies showed that CVS and GVS produce transient remission of hemianaesthesia in brain-damaged patients [13,14,15,16].

However, both CVS and GVS involve unnatural peripheral stimulation. They activate not only classically 'vestibular' and multisensory areas, but also attentional and visuo-spatial processing regions [5,17]. Thus, at least two possible mechanisms could underlie vestibular-somatosensory interactions observed with CVS and GVS. First, vestibular stimulation might modulate somatosensory processing, for instance via neurons receiving both vestibular and somatosensory signals (Figure 1b) [10]. Alternatively, vestibular stimulation might influence somatosensory perception *indirectly*, via a supramodal spatial attentional mecha-

nism [13,14] (Figure 1a). This alternative indirect hypothesis is plausible given the strong effects of vestibular inputs in orienting of spatial attention [18] and in orienting behaviours generally [19]. Thus, it is important to identify whether vestibular effects on the somatosensory system are spatially-selective or not.

Studies describing the vestibular induced modulation of tactile processing suggested a direct vestibular interaction with somatosensory circuits [8,9,10]. Interestingly, the changes in the somatosensory thresholds and sensitivity were found on both left and right hand following unilateral vestibular activation. However, previous experiments cannot rule out additional non-specific effect of vestibular stimulation on somatosensory processing, because of the strong effects of artificial vestibular stimulation. For example, vestibular stimulation could influence performance because of general arousing effects, or by shifts of spatial attention. The former hypothesis has been ruled out by a number of studies using artificial vestibular stimulation to compare generic effects, resulting from stimulation of either hemisphere, to hemisphere-specific effects obtained with particular lateralisation of stimulation [15,16]. For example, it has been recently reported that hemisphere-selective left anodal and right cathodal polarity of GVS significantly enhanced sensitivity to mild shocks on either hand, while no such effect was found with either right anodal and left cathodal GVS or sham stimulation [9]. These hemisphere-specific effects cannot readily be explained by general arousal, since the peripheral vestibular organs receive comparable stimulation in both cases. In contrast, artificial vestibular stimulation studies are less able to rule out accounts based on spatial attention, because they cannot precisely control the spatial aspects of the stimulation.
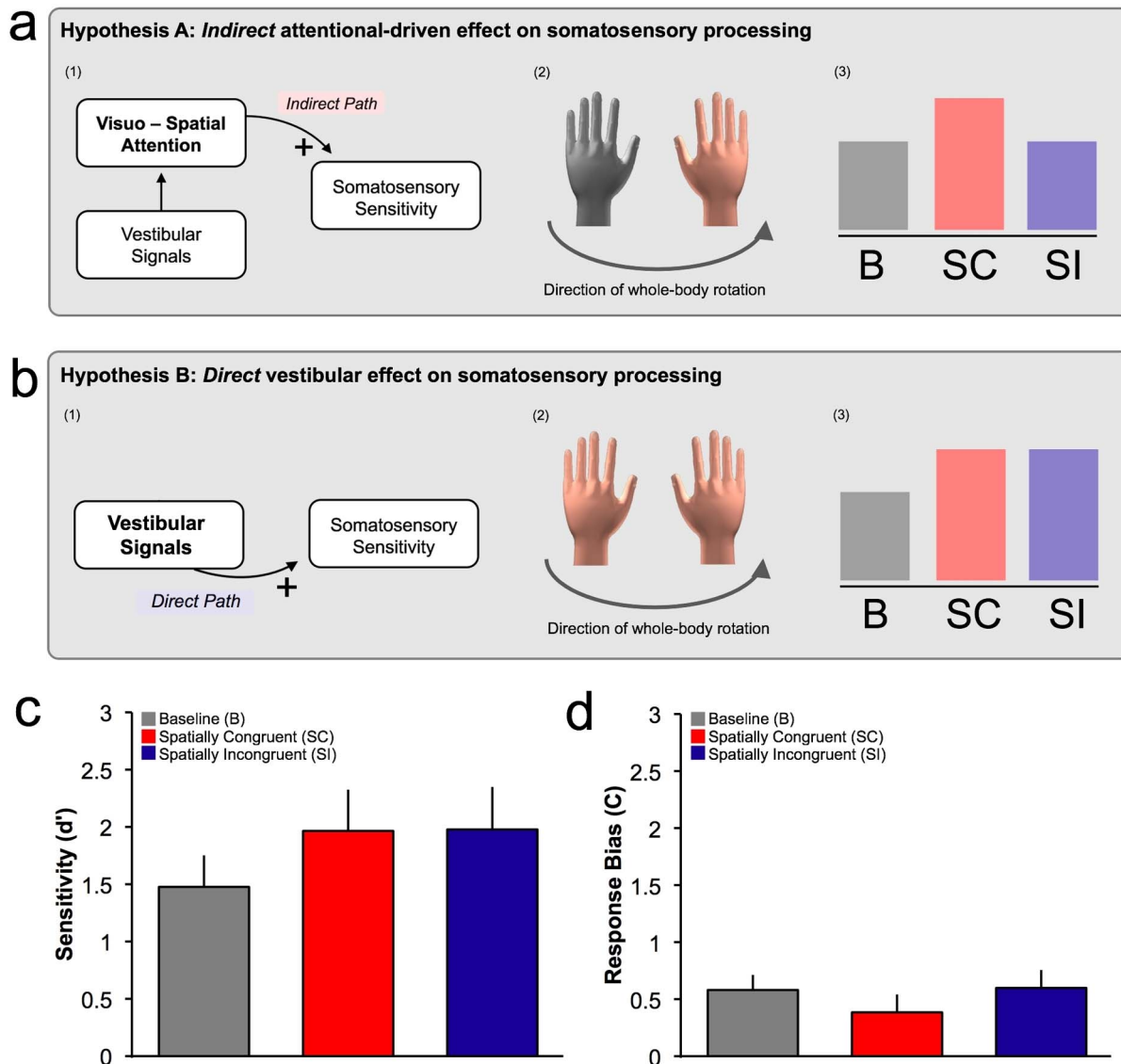
Figure 1. Experimental hypotheses and results. Experimental hypotheses are illustrated in panel (a) and (b). (a1) Somatosensory processing might be modulated by an *indirect* attentionally-mediated (spatially-selective) effect of vestibular stimulation. An indirect effect on somatosensory processing predicts an improved tactile sensitivity only when touch and rotation are spatially congruent, e.g., touch on the right hand and rotation toward the right (a2). In particular, the indirect effect (a3) would induce no improvement in tactile sensitivity between a no rotation Baseline condition (B) and Spatially incongruent condition (SI), but a selective enhancement of sensitivity in the Spatially congruent condition (SC). Alternatively, (b1) somatosensory processing might be directly (non spatially-selective) influenced by vestibular signals. This predicts an enhancement of tactile sensitivity independent of the spatial relation between location of touch and direction of rotation (b2). In particular, this effect (b3) would not predict differences in sensitivity between Spatially congruent condition (SC) and Spatially incongruent condition (SI), critically it predicts that both conditions (SC and SI) would be different compared to Baseline condition (B). (c) Sensitivity (d′) data as a function of experimental conditions. d′ estimates support the hypothesis of a direct vestibular induced modulation. (d) Response bias (C) data as a function of experimental conditions.
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Here we investigated the vestibular enhancement of tactile processing using a *natural* activation of vestibular cortical projections, through passive whole-body yaw rotation. This method of stimulation permits precise control over the spatial signals generated in the peripheral vestibular system, and therefore over spatial congruency/incongruency. It allowed us to test whether vestibular effects on tactile perception were present also with this more natural stimulation, and whether they were spatially-selective or not.

Spatially-selective perceptual mechanisms have been reported in neurons responding to visuo-auditory [20], visuo-tactile [21], and visuo-vestibular stimuli [22,23]. For instance, stimuli signalling motion in complementary directions (e.g. vestibular rotation to the right and optic flow to the left) are preferentially integrated. Multisensory neurons coding for visual, vestibular and somatosensory stimuli were found in the macaque ventral intraparietal area (VIP) [24], homologous to human vestibular areas in the posterior parietal cortex [17]. Importantly, the firing patterns of the majority of VIP neurons showed a preference for ipsiversive

stimuli: for instance, a bimodal neuron receiving both tactile and vestibular signals would preferentially responds to rightward rotation and to touch on the right cheek. One could thus imagine that the processing of tactile stimuli will be facilitated when coupled with vestibular rotation in the same direction.

A somatosensory detection task was administered during passive whole-body rotations. Participants sat on a rotating chair and were instructed to detect faint tactile shocks delivered to the left or to the right hand. Direction of rotation and tactile stimulation conditions were independently randomized. This orthogonal design ensured that spatial-attentional effects of congruency/incongruency could be estimated directly, and were never predictable. Recent studies [18] revealed that passive whole-body rotatory accelerations produce spatiotopic shifts of attention in the direction of rotation (i.e, congruent or ipsiversive direction), which moreover influence tactile detection. We hypothesized that an *indirect* modulation of tactile sensitivity mediated by this shift of spatial attention would produce an improved detection for faint shocks delivered to the hand spatially congruent to the direction of rotation (Figure 1a), compared to the other hand. Alternatively, we might observe non spatially-selective effects of vestibular stimulation on somatosensory detection, independent of the spatial congruency between touch and rotation (Figure 1b).

Methods

1. Ethics Statement

The experimental protocol was approved by the local ethics committee (École Polytechnique Fédérale de Lausanne) and the study was conducted in line with the Declaration of Helsinki. Participants gave written informed consent to participate in the experiment before inclusion in the experiment.

2. Participants

Fifteen naïve paid right-handed participants volunteered in the experiment (10 male, ages: 19–36 years, mean ± SD: 23.67±4.51 years). Handedness was assessed through informal verbal inquiry. Data from three participants was discarded due to an inability to correctly estimate reliable sensory thresholds (see below for further details).

3. Experimental Procedure

The experiment was conducted in complete darkness in a sound-shielded room in which a human motion platform was placed (see also [25]). Whole-body passive rotations were performed around the yaw axis by placing participants in a chair mounted on a two meters beam platform fixed on a digitally controlled electrical engine. The system (PCI-7352) operates with a precision of $+/-0.1$ deg/sec for a peak acceleration of $400°/s^2$ $(+/-6$, torque $>2kNm)$. Participants were seated in the chair wearing seatbelts, with their head aligned to their body's z axis and precisely located in the center of rotation. An adjustable chin-rest fixed the head position. An infrared surveillance camera monitored the subjects' face continuously.

Participants were instructed to detect faint tactile pulses during whole-body passive rotations, and in a baseline condition involving no rotation. Since the motion platform produces slightly vibrations, the no-rotation trials were performed with motion platform powered on. This procedure insures that non specific-vestibular cues, such as vibrations of the motion platform, were equally present across experimental conditions, even if the rotator was not turning. Although the no-rotation trials controlled for platform vibrations, other bodily proprioceptive cues might be associated with whole-body rotation. Tactile electrical stimulation was

delivered via a pair of ring electrodes placed over the distal phalanxes of the index fingers of both hands, with the cathode 1 cm proximal to the anode. Stimulation was delivered with a neurophysiological stimulator (Grass S48 stimulator), whose current level and pulse duration were manually controlled. To identify individual somatosensory thresholds, a staircase procedure was used to estimate the lowest shock intensity at which a tactile stimulus could be reliably detected. Independent thresholds were estimated for each participant's left and right fingers. Pulse intensity obtained with the thresholding procedure was successively tested in a detection block and adjusted until the 40–60% of pulses were reliable detected on both fingers. This level was considered as working estimate for near threshold electrical stimulation in each participant.

Our design factorially combined passive body rotation and tactile stimulation conditions (see Table 1). Every trial involved a single rotation (if present), during which a single shock (if present) would be delivered. In particular, we were interested in three experimental conditions: (i) *Baseline condition*, in which the shock was delivered either to the left or right index finger without passive whole-body rotation; (ii) *Spatially congruent condition*, in which the shock was delivered to the hand congruent to the direction of rotation (i.e. shocks delivered to the left finger during left direction whole-body rotation and shocks delivered to the right finger during right direction whole-body rotation), (iii) *Spatially incongruent condition*, in which the shock was delivered to the hand opposite to the direction of rotation (i.e., shocks delivered to the left finger during right direction whole-body rotation or shocks delivered to the right finger during left direction whole-body rotation).

The somatosensory detection task was designed following a signal detection approach [26]. It consisted of six tactile stimulus-present trial types: 15 trials with a shock delivered to the left hand during no rotation; 15 trials with a shock delivered to the right hand during no rotation; 15 trials with a shock delivered to the left hand during leftward spatially congruent rotation; 15 trials with a shock delivered to the right hand during rightward spatially congruent rotation; 15 trials with a shock delivered to the left hand during rightward spatially incongruent rotation and 15 trials with a shock delivered to the right hand during leftward spatially incongruent rotation. There were also six corresponding trial types in which no tactile stimulus was delivered, during the same rotation conditions. Notice that separate sets of 15 trials were used to define conditions in which no shock was delivered to the left hand and in which no shock was delivered to the right hand – this allowed separate 'no stimulus' trials to be used to calculate the signal detection parameters for each hand. A total of 180 trials were performed and divided in five experimental blocks. Trial order was randomized, so that participants could not predict tactile stimulus presence, hand stimulated or rotation direction. Before each experimental block a pre-test sensory detection block was administered to check the stability of the perceptual sensory threshold.

Participants were asked to fixate a white cross, centred on a 22″ computer screen mounted on the chair 40 cm in front of the eyes. The beginning of each trial was signalled by a change in the colour of the fixation cross, which became red. The rotation, if present, started after 2000 ms from the beginning of the trial. The chair's rotation profile consisted of 1000 ms acceleration to a speed of $90°/s$, followed by 1000 ms deceleration to $0°/s$ (raised cosine). For each block a different rotation profile was generated. The profile varied by randomized direction of rotation. The shock, if present, was delivered 2700 ms from the beginning of the trial. Thus, during the whole-body rotation trials the shock was delivered at 700 ms from the onset of acceleration, to coincide

Table 1. Experimental conditions and stimulus design.

	Tactile stimulation	
Direction of Rotation	*Left hand*	*Right Hand*
No rotation	Baseline condition	Baseline condition
Leftward rotation	Spatially congruent condition	Spatially incongruent condition
Rightward rotation	Spatially incongruent condition	Spatially congruent condition

Passive body rotation and tactile stimulation conditions were factorially combined to provide independent estimates of direct vestibular modulation and indirect effects driven by factors such as attention. Every trial involved a single rotation (if present) during which a single shock (if present) would be delivered to the left or right hand.
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with the reported maximal firing of vestibular afferents. Participants were required to indicate whether or not they felt the shock, making un-speeded verbal responses ('yes' or 'no') during a response window of 4000 ms in which the fixation cross was green. During the experiment white noise was presented over the participants' headphones and a black blanket covered the chair, to avoid the participant from inferring the rotation direction based on auditory or visual cues (residual light emanating from the stimulus display). Data for each trial were recorded and analysed later.

Results

Tactile detection results were analysed using signal detection analysis [26]. The number of hits (number of tactile stimulus-present trials in which participants said 'yes'), false alarms (number of stimulus-absent trials in which participants said 'yes'), misses (number of stimulus-present trials in which participants said 'no') and correct rejections (number of stimulus-absent trials in which participants said 'no') was computed for each experimental condition (Baseline condition, Spatially congruent condition and Spatially incongruent condition). These values were used to obtain the perceptual sensitivity (d') and response bias (C) estimates.

A 3x2 repeated measure ANOVA with factors of Condition (Baseline condition, Spatially congruent condition, Spatially incongruent condition) and Side of tactile stimulation (Left finger, Right finger) were performed on d' and C estimates. Analysis of d' values showed a just-significant effect of Condition $(F_{(2,22)} = 3.469, p = 0.049)$. There was no effect of Side of tactile stimulation $(F_{(1,11)} = 1.592, p = 0.233)$ and no interactions between factors $(F_{(2,22)} = 1.325, p = 0.286)$. Post hoc t-tests were used to explore the main effect of Condition, holding the level of each factor constant and investigating the effects of the other factor. These contrasts revealed a significant difference between Baseline condition and Spatially congruent condition $(t(11) = -2.335, p = 0.040)$ and also between Baseline condition and Spatially incongruent condition $(t(11) = -2.307, p = 0.042)$, but no significant difference between Spatially congruent condition and Spatially incongruent condition $(t(11) = -0.058, p = 0.955)$. Note that correction for multiple comparisons is not generally recommended for the specific case of comparison between three conditions following significant omnibus ANOVA. Analysis of response bias (C values) showed no significant main effect of Condition $(F_{(2,22)} = 1.816, p = 0.186)$, or Side of tactile stimulation $(F_{(1,11)} = 3.794, p = 0.077)$, and no significant interaction between factors $(F_{(2,22)} = 2.385, p = 0.115)$.

Discussion

The vestibular system has widespread interactions with other sensory modalities, including somatosensory signals. Multisensory

neurons responding to vestibular and tactile stimulation were found in primate posterior parietal cortex (area VIP) [24], where the majority of the recorded cells encoded stimuli moving in the same direction. Another region in posterior parietal cortex (area 2v) immediately adjacent to primary somatosensory areas of hand and mouth also responds to vestibular stimulation coming from the semicircular canals and the otolith organs [27,28]. Bimodal neurons coding for vestibular and tactile stimulation were also described in the so-called parieto-insular vestibular cortex (PIVC) [29] and such neurons responded to vestibular stimulation as well as touch applied on the arms, shoulders, neck, and legs. These findings were recently extended to humans: both caloric and galvanic artificial vestibular stimulation increased somatosensory sensitivity and modulated somatosensory potentials evoked by median nerve stimulation [8,9,10].

Here we observed that natural vestibular inputs elicited by passive whole-body rotation also enhanced tactile sensitivity. Importantly, this increase was independent from the spatial congruency between the direction of the rotation and the hand stimulated, since we found no evidence for a difference in the tactile sensitivity depending on whether the left or right finger received tactile stimulation during left or right passive whole-body rotations. Further, our data revealed that response bias is not affected by passive whole-body rotation. These results follow the predictions of a spatially non-selective vestibular-somatosensory interaction, and fail to follow the predictions of a spatially-selective vestibular-somatosensory interaction mediated by shifts in spatial attention or by spatially-selective perceptual mechanisms.

Vestibular stimulation has been often associated with shifts of spatial attention. Clinical reports in patients with circumscribed right hemispheric brain damage interpreted effects of artificial vestibular stimulation on tactile perception in terms of shifts of supramodal spatial attention toward the side of the space ipsilateral to the vestibular organs stimulated [13,14]. Similarly, a recent study in healthy participants showed that vestibular stimulation by whole-body rotatory accelerations produces ipsiversive shifts of attention [18]. It is important to note that the experimental setup used in that study differed from the present study in important respects. First, the duration of rotation was much longer (6 s, compared to 2 s in the present study). Second, the stimuli were presented later during the acceleration phase (1500 ms after the beginning of rotation), than the stimuli in the present study. Our stimuli were presented at the peak of the acceleration phase (700 ms after the beginning of rotation). Third, the no-rotation interval between trials was much longer than in our experiment (15 s, in comparison to 6 s in the present study). Fourth, the tactile stimuli were well above threshold, whereas we used near-threshold stimuli. Fifth, Figliozzi et al. (2005) [18] asked participants to perform temporal order judgements rather than detection. Finally, the participants made manual responses

whereas our study used unspeeded vocal responses. We can only speculate how all these various factors may influence the direct and indirect interactions between vestibular and somatosensory systems. However, we believe that the last point might explain the discrepancy between the results. Critically, Figliozzi et al. (2005) [18] used manual response keys placed along the direction of rotation. This was absent in our study, in which simple verbal responses were recorded. We therefore speculate that indirect mechanisms based on selective attention may dominate vestibular-somatosensory interactions when salient stimuli are processed and central motor plans are activated [18]. In contrast, direct vestibular-somatosensory interactions may be more important for perceptual processing close to threshold. In summary, our results cannot easily be reconciled with a spatially-selective attentional interpretation. Accounts based on *indirect,* attentional mechanisms would predict facilitatory effects on tactile detection only during spatially congruent rotations. Thus, during the present yaw rotation attention would be oriented toward the side of space and body congruent with the direction of the yaw rotation. However, our data did not reveal any difference between rotation directions both in tactile sensitivity and response bias.

In contrast, our study provides evidence for a direct vestibular-somatosensory interaction, independent of any modulation of rotation-dependant spatial attention or spatial perceptual mechanisms. Our results showed that natural vestibular stimuli elicited by passive whole-body yaw rotations produced an increase in tactile sensitivity similar to the effects described previously with artificial vestibular stimulations [8,9]. Although the vestibular activations elicited by natural versus artificial vestibular stimulation are very different. At the peripheral level, the vestibular system is composed by three orthogonal semicircular canals detecting rotational movements of the head in the three-dimensional space (i.e., pitch, yaw and roll) and with two otolith organs (utricle and saccule) detecting translational acceleration, including the gravitational vertical. Artificial vestibular stimulations produce strong activations of both semicircular canals and otolith organs, while passive whole-body rotation as used here selectively stimulates the semicircular canals. Our results using yaw rotations suggest that the stimulation of canal-dependant rotational vestibular signals is sufficient to influence somatosensory processing.

Both somatosensory cortical areas and the insular cortex were found to respond to vestibular and somatosensory inputs in human neuroimaging studies, indicating an anatomical basis for the multisensory interaction between the two sensory modalities [3,4,5,6]. We suggest that vestibular inputs could act to increase the firing of neurons responding to somatosensory input, thus enhancing somatosensory detection. Convergence of vestibular and tactile inputs onto bimodal neurons in these areas is one possible mechanism for this enhancement [30].

Caution is required in interpreting the non significant interaction that we found between direction of rotation and hand stimulated. Absence of interaction suggests that leftward and rightward rotations have similar effects on tactile sensitivity. This lack of lateralization is in contrast with previous findings using artificial vestibular stimulation, which found stronger somatosensory effects following vestibular stimulation designed to activate

the vestibular network in the right hemisphere (i.e., left cold CVS [8]; left anodal and right cathodal GVS [9]). Neuroimaging studies using GVS identified the same asymmetry in the cortical vestibular system, suggesting that the cortical vestibular network is primarily located in the non-dominant right hemisphere in right-handed subjects [31]. However, the present data suggest that such hemispheric lateralisation induced by CVS and GVS might be related to the unusual unilateral nature of the artificial stimulation. During the natural rotatory stimulations used here, both left and right vestibular peripheral organs are activated, so that the input should be balanced across hemispheres. Thus, differences between the types of vestibular stimulation used and the consequent activations of vestibular afferents might explain the contrasting findings from artificial and natural vestibular stimulation. Natural vestibular stimulation produces balanced vestibular inputs to the two hemispheres, and shows spatially non-selective interactions with somatosensation. In contrast, existing methods of artificial vestibular stimulation involve a lateralised peripheral stimulus, both to the vestibular organs, and to other sensory receptors. For example, in many CVS studies, cold water is placed in the left ear. This not only activates the vestibular organ, but also provides a lateralised thermal and tactile stimulus. Spatially-selective effects of vestibular stimulation on other modalities might therefore, in principle, be due either to vestibular involvement in spatial attention, or to attentional effects of lateralised stimulation.

Could the enhancement in somatosensory sensitivity alternatively be an indirect effect of passive whole-body yaw rotation? For example, passive whole-body rotation might have increased general arousal. Our data cannot conclusively exclude this hypothesis. However, we believe an explanation based on arousal is unlikely for two reasons. First, some other sensory modalities such as vision [32] and nociception [33] are inhibited by artificial vestibular stimulation, in contrast to the facilitation of touch that we have reported. This speaks against a general arousal effect. Second, the natural vestibular stimulation in this experiment is similar to those encountered in everyday experience. Such natural head rotations do not seem to produce dramatic changes in arousal. However, further systematic investigation is required to investigate a possible role of arousal in vestibular-somatosensory interaction.

Conclusion

Previous studies have focussed on the clinical [13,14], anatomical [4,6] and perceptual [8,9] aspects of vestibular-somatosensory interactions as tested by unnatural vestibular stimulation. Here we show that naturally-evoked vestibular signals enhance near-threshold somatosensory processing. Our results are compatible with a direct and spatially non-selective modulation of somatosensory processing by concurrent vestibular input. Our results cannot readily be explained by changes in spatially-selective attention related to rotation.

Author Contributions

Conceived and designed the experiments: ERF PH OB. Performed the experiments: MK ERF BH. Analyzed the data: ERF MK. Wrote the paper: ERF PH OB MK BH.

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Study 4: Multisensory effects on somatosensation: a trimodal visuo-vestibular-tactile interaction

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Brief Communication

Multisensory effects on somatosensation: a trimodal visuo-vestibular-tactile interaction

Abbreviated title: Visuo-vestibular-somatosensory interaction

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Abstract

Vestibular information about self-motion is combined with other sensory signals. Previous research described both visuo-vestibular and vestibular-tactile bilateral interactions, but the simultaneous interaction between all the three sensory modalities has not been explored. Here we exploit previously reported visuo-vestibular integration to investigate multisensory effects on tactile sensitivity. Tactile sensitivity was measured during passive whole body rotations alone or in conjunction with optic flow, creating either purely vestibular or visuo-vestibular sensations of self-motion. Our results demonstrate that tactile sensitivity is modulated by perceived self-motion, as provided by a combined visuo-vestibular percept, and not by the visual and vestibular cues independently. We propose a hierarchical multisensory interaction that underpins somatosensory modulation: visual and vestibular cues are first combined to produce a self-motion percept. Somatosensory processing is then enhanced according to the degree of perceived visuo-vestibular self-motion.

Introduction

Self-motion detection and maintaining postural stability require combination of vestibular with visual and somatosensory signals, such as retinal optic flow, shifts of body weight and the quality of body contact with the supporting surface (Mergner and Rosemeier, 1998; Rogers et al., 2001; Wexler et al., 2001; Logan and Duffy, 2006). Visuo-vestibular integration underlies perception of whole body rotations and translations (Fetsch et al., 2009; Prsa et al., 2012), even when visual and vestibular stimuli are in conflict (Wright et al., 2005; Ishida et al., 2008; Kaliuzhna et al., 2015).

Caloric (CVS) and galvanic (GVS) vestibular stimulation, and natural vestibular stimulation from passive whole-body rotations all increase tactile sensitivity in healthy participants (Ferrè et al., 2011a; Ferrè et al., 2013b; Ferrè et al., 2014). CVS and GVS also transiently improve tactile deficits in neurological patients (Vallar et al., 1990; Vallar et al., 1993; Kerkhoff et al., 2011; Schmidt et al., 2013). Anatomically, visual, vestibular and tactile signals converge at the level of the vestibular nuclei (Waespe and Henn, 1978), at the thalamus (Sans et al., 1970; Magnin and Putkonen, 1978) and in multisensory cortical regions such as the parietal operculum and the posterior insula (Schwarz and Fredrickson, 1971; Grüsser et al., 1990; Bremmer et al., 2002; Lopez, 2013).

Despite the close anatomical and behavioural connections between visual and vestibular cues on the one hand, and vestibular and tactile on the other, the *trimodal interaction* between them remains unexplored. In particular, it is unclear whether vestibular-tactile interactions are merely a by-product of anatomical convergence in the cortex, or instead depend on perceptual representation of environmental self-motion.

Here we investigated visuo-vestibular-tactile interactions in healthy volunteers. Specifically, we explored whether the vestibular effect on touch is a direct consequence of vestibular stimulation or whether it rather depends on prior integration of vestibular and visual signals forming a self-motion representation, that subsequently influences touch (Figure 1b). Participants detected faint tactile stimuli delivered to either their left or right index fingers in three conditions: a static baseline

condition, during passive whole-body rotation (vestibular condition), and during passive whole-body rotation in the presence of visual optic flow (visuo-vestibular condition). Crucially, vestibular input was identical in the two rotation conditions, but the perceived velocity of self-motion was reduced in the third condition by concurrent optic flow. If the influence of vestibular signals on tactile detection is a by-product of a direct anatomical vestibular-somatosensory convergence, we should observe identical vestibular modulations of touch in both rotation conditions, whether visual motion is present or not (Figure 1b). If, however, tactile detection is modulated by an integrated visuo-vestibular signal then tactile enhancement should differ between vestibular conditions, due to slow-velocity optic flow (Figure 1b).

Materials and Methods

Participants

Fourteen naïve paid right-handed participants took part in Experiment 1 (mean age 25.1 years, SD=3.7 years, 5 females) and in Experiment 2 (mean age 25.2 years, SD=3.6 years, 2 females). The study was conducted in line with the Declaration of Helsinki. The experimental protocol was approved by the local ethics committee (École Polytechnique Fédérale de Lausanne). Participants gave written informed consent in advance. All participants were right-handed as assessed by informal verbal inquiry.

Procedure

Experiment 1 tested for the effects of visuo-vestibular integration on tactile detection. Experiment 2 controlled for possible effects of visual optic flow on tactile detection in the absence of vestibular signals. The same experimental setup was used for both experiments.

Experiment 1: Visual and vestibular effects on tactile detection.

We made two predictions as to the vestibular and visuo-vestibular effects on touch (Figure 1b). A direct vestibular–somatosensory interaction would predict similar increases in tactile sensitivity in both the vestibular and visuo-vestibular conditions. Interaction between a combined visuo-vestibular self-motion signal and somatosensation predicts lower tactile sensitivity in the visuo-vestibular condition, as compared to the vestibular condition.

Participants were seated inside a sound-shielded dark room in a custom-built centrifuge cockpit-style chair which delivered passive whole body yaw rotations (c.f., Van Elk, 2013; Prsa et al., 2012). Head and body motion were prevented by using head fixation, a restraining harness and cushioning. The chair was digitally servo-controlled (National Instrument PCI-7352) with +/- 0.1° precision. The chair rotated in the yaw plane and was centred on the rotation axis, thus delivering only angular acceleration vestibular stimuli. The rotation profiles of the chair were pre-set to 1000ms of acceleration (raised cosine) to 90°/s followed by 1000ms deceleration to 0°/s. Having previously shown that 90°/s yaw rotations increase tactile sensitivity (Ferrè et al., 2014), we employed the same velocity for the present experiment. Yaw rotation was in either clockwise or counter-clockwise direction.

Participants wore a head-mounted display showing a central fixation cross and an optic flow stimulus (3D pattern of moving dots). The velocity of the optic flow was set to 10°/s on the basis of a pilot experiment. Briefly, in this pilot experiment, participants (N=14, mean age 26.1 years, SD=4.2 years, 2 females) judged the perceived speed of their displacement on a scale from 0 to 100, using a joystick. The chair rotated at 90°/s, while one of four visual speeds (10, 30, 45 and 90°/s) was presented in either congruent (e.g. 90°/s vestibular rotation clockwise paired with 10°/s optic flow clockwise) or incongruent directions (the 90°/s speed was presented only in the congruent direction). A vestibular only control condition, without optic flow, was also tested. Each condition was repeated 20 times. The visual stimulus that most strongly influenced perceived velocity was the 10°/s velocity-

incongruent condition. This significantly reduced the perceived velocity of self motion (mean scale units=55.1, SD=14.7) relative to a no visual stimulation condition (mean=68.6, SD=13.4): t(13)=-4.3, p=0.0008. We thus selected the 10°/s velocity incongruent optic flow as the visual stimulus to test our main hypotheses in Experiments 1 and 2.

The direction of optic flow motions was always counterdirectional with respect to the direction of chair rotation. That is, when vestibular information specified a clockwise rotation at 90°/s, the counter-clockwise visual flow also specified a clockwise rotation, but at only 10°/s. Thus, the two stimuli were congruent regarding the direction of rotation, although they specified different velocities. Therefore, if participants integrated the visual and vestibular information about velocity, the perceived rotation velocity should be slower when visual stimulation was present than when it was not. Participants were asked to fixate the fixation cross at all times. The beginning of a trial was signalled by a change in colour of the fixation cross (from white to red). Trials were separated by 5 or 6 s of no rotation periods. Visual stimuli were generated by in-house software (ExpyVR).

Participants were asked to detect faint tactile stimuli delivered to the distal phalanxes of their index fingers by solenoid tappers in different experimental conditions (Ferrè et al., 2014). Stimulation intensity was manually adjusted following a staircase procedure to identify a threshold of 40-60% detection rate, which was then validated in an automated detection block. This level of intensity was then used during the experiment.

Our design factorially combined passive body rotation, optic flow and tactile stimulation conditions. Every trial involved a single rotation (if present), during which a single shock (if present) would be delivered. In particular, we were interested in three experimental conditions: (i) No rotation *baseline condition*, in which the shock was delivered either to the left or right index finger without passive whole-body rotation; (ii) *Vestibular condition*, in which the shock was delivered during 90°/s yaw whole body rotation, (iii) *Visuo-vestibular condition*, in which the shock was delivered during 90°/s yaw rotation with velocity incongruent optic flow of 10°/s (Figure 1a).

The tactile detection task was designed using a signal detection approach (Macmillan and Creelman, 2004); for each condition, the stimulus was present in 30 trials and absent in another 30 trials. In the vestibular and visuo-vestibular conditions 16 tactile stimuli were delivered to the right hand (half during clockwise and half during counter clockwise rotation) and 14 tactile stimuli to the left hand (half during clockwise and half during counter clockwise rotation). For the catch trials, the same number (15) of clockwise and counter clockwise rotations was used. In the baseline condition 15 tactile stimuli were delivered to the left hand and 15 to the right hand. Participants thus performed a total of 180 tactile detection trials, divided into five blocks, and presented in a randomised order. The presence or absence of the stimulus, the hand stimulated and the direction of rotation were unpredictable. Before each block, the tactile detection threshold was checked and adjusted if required.

The tactile stimuli, when present, occurred 700ms after the onset of acceleration, i.e. at peak rotation velocity. At the end of the trial (trial duration: 2000ms) participants had 4000ms to verbally report (yes-no response) whether they felt the tactile stimulus. They were asked to fixate a green fixation cross throughout the block. When the fixation cross turned white, participants were asked to respond. During the baseline and vestibular conditions only the fixation cross appeared in the HMD. During the experiment white noise was presented over the participants' headphones and a black blanket covered the chair, to avoid participants' inferring the rotation direction from auditory or visual cues. Data for each trial were recorded and analysed later.
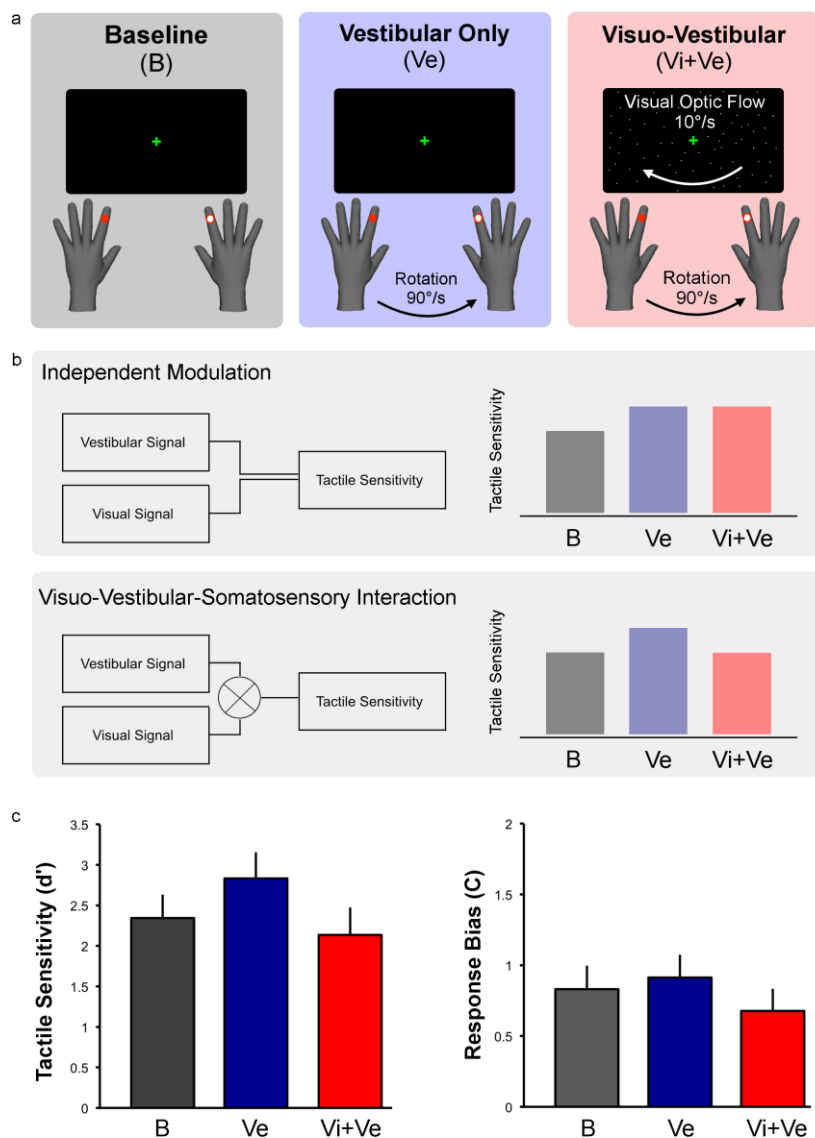
Figure 1. Experimental conditions and results

(a) Experimental conditions for Experiment 1. Participants were seated in the rotating chair wearing a head-mounted display showing (or not) a pattern of moving dots. Participants were asked to detect faint tactile stimuli delivered to their index fingers. Three conditions were tested: no rotation baseline (B), vestibular only condition (Ve, passive whole-body rotations at 90°/s) and visuo-vestibular condition (Vi+Ve, passive whole-body rotation at 90°/s associated with velocity incongruent optic flow at 10°/s).

(b) Experimental hypothesis. If the influence of vestibular signals on tactile detection is a direct product of the activation of the vestibular projections, data should show an increase in

somatosensory sensitivity in both Ve and Vi+Ve conditions (independent modulation hypothesis). Conversely, if somatosensory sensitivity is affected by integrated visual and vestibular signals leading to the perception of slower speed, tactile enhancement should be reduced in the Vi+Ve condition, relative to Vi (visuo-vestibular-somatosensory interaction).

(c) Sensitivity (d') and response bias (C) data as a function of experimental condition. Results show higher sensitivity in the vestibular only condition as opposed to the baseline and visuo-vestibular conditions. No difference was found between the latter two. There were no significant differences in response bias.

Experiment 2. Independent effects of optic flow on tactile detection.

This experiment controlled for any independent effects of optic flow on tactile detection, i.e. in the absence of vestibular stimulation. Tactile detection was tested during two conditions: with and without 10°/s optic flow stimulation. Participants were placed in the rotating chair, which was always stationary but was powered on as during Experiment 1. The optic flow used was the same as in Experiment 1 and on half of the trials simulated clockwise rotation, and on the other half counter-clockwise rotation. Participants performed a total of 120 trials; for each condition the tactile stimulus was present in 30 trials and absent in the other 30 trials. The experiment was divided into three blocks.

Results

Experiment 1: Visual and vestibular effects on tactile detection.

Signal detection analysis was applied to the tactile detection results, allowing us to extract perceptual sensitivity (d') and response bias (C) estimates for each participant and condition. These values were subjected to an ANOVA comparing the three experimental conditions (baseline, vestibular and visuo-vestibular). The main effect of experimental conditions was found to be

significant for sensitivity values (F(2, 26)=3.6895, p=0.039) and two tailed post-hoc t-tests showed significantly better sensitivity in the vestibular condition compared with the baseline condition (t(13)=-2.28, p=0.04), no such difference between baseline and the visuo-vestibular condition (t(13)=0.71, p=0.5), and significantly better sensitivity in the vestibular condition compared with the visuo-vestibular condition (t(13)=2.53, p=0.03). No correction for multiple comparisons is required for post-hoc tests following a significant omnibus ANOVA with three conditions (Cardinal and Aitken, 2013). No significant differences were found for the response bias (F(2, 26)=1.3616, p=0.3) (Figure 1c).

Experiment 2: Independent effects of optic flow on tactile detection.

Sensitivity and response bias were estimated for each experimental condition. The mean sensitivity value for the baseline condition was 2.16 (SD=0.98) and 2.15 (SD=1.07) for the optic flow condition. Mean response bias values were 0.96 (SD=0.57) and 0.83 (SD=0.57) accordingly. Two tailed t-tests showed no significant difference between the baseline and optic flow conditions for neither sensitivity (t(13)=0.033, p=0.97) nor response bias (t(13)=0.77, p=0.46).

Discussion

The tentacular nature of cortical projections from the peripheral vestibular organs might underlie the interactions that vestibular signals have with other sensory modalities. The combination of visual, vestibular and somatosensory information ensures self-motion detection (Berthoz et al., 1975; Bremmer et al., 1999; Siegler et al., 2000), postural stability (Dichgans and Brandt, 1978; Horak et al., 1994) and spatial orientation (Lackner and DiZio, 2005; Villard et al., 2005; Clement et al., 2009; Ferrè et al., 2013a). Recent behavioural, neuropsychological and psychophysiological studies have confirmed these close visuo-vestibular interactions (Fetsch et al., 2009; Butler et al., 2010; Prsa et al.,

2012) as well as vestibular-tactile interactions (Vallar et al., 1990; Ferrè et al., 2011a; Ferrè et al., 2011b; Ferrè et al., 2013b; Ferrè et al., 2014).

We provide further evidence for increased tactile sensitivity during different forms of vestibular stimulation, extending previous findings as shown with CVS and GVS (Ferrè et al., 2011a; Ferrè et al., 2013b), and yaw rotations (Ferrè et al., 2014). Crucially, the effect of yaw rotation on touch was reduced in the present visuo-vestibular condition. Thus, when velocity incongruent visual and vestibular signals were combined (producing a slower perception of self-rotation), tactile detection deteriorated relative to a vestibular only condition, and was no longer enhanced relative to baseline. Thus, in the visuo-vestibular condition tactile sensitivity was significantly worse than in the vestibular alone condition, despite identical yaw rotations in these two conditions. Two explanations could account for these results. On the one hand, tactile detection could be influenced by an integrated percept of visual and vestibular stimuli. On the other hand, vestibular and visual information could independently and simultaneously affect tactile detection. In this case an effect of optic flow alone on tactile detection should be observed: 10°/s optic flow stimuli (as tested here) should reduce tactile sensitivity. Experiment 2 ruled out this latter possibility. We found no effect of 10°/s velocity optic flow on tactile sensitivity as compared to a baseline without rotation or optic flow.

Our results demonstrate that somatosensory processing in the presence of a visuo-vestibular combination is not driven by the vestibular stimulus directly, nor by two independent and direct inputs from visual and vestibular organs. Our result also rules out the possibility that somatosensory facilitation is just due to a non-specific factor of stimulus-evoked arousal. An account based on arousal would predict stronger somatosensory facilitation in the visuo-vestibular condition than in the vestibular alone condition, because of the additional visual stimulation. In fact, we found a significant effect in the opposite direction.

Instead, we suggest that the integrated visuo-vestibular stimulus that specifies self-motion influences somatosensation. Visual and vestibular signals necessarily combine for ocular-motor stabilisation

(Jahn et al., 2002), and are inevitably congruent in everyday life during self-motion. In addition, previous research demonstrates that visuo-vestibular stimuli signalling self-motion are fused into a single representation, such that the individual visual and vestibular cues are no longer accessible to the system (Prsa et al., 2012). In contrast, tactile information on the hands might be irrelevant to self-motion (i.e. texting on a mobile phone while walking) and thus should not be automatically integrated with vestibular cues. Finally, it might be that in daily life visual and vestibular signals co-occur more frequently than, say, vestibular-tactile signals (e.g. moving one's head more frequently when stationary (seated) or during passive displacement than during active self-motion) and even less so for tactile stimuli on the surface of the fingers.

The anatomical locus of this influence remains speculative. Some neurons that integrate both vestibular stimulation and optic flow are found as early in the processing stream as the vestibular nuclei and the thalamus (Magnin and Putkonen, 1978; Waespe and Henn, 1978). Visual, vestibular and somatosensory signals thereafter overlap at multiple levels. Vestibular neurons in the thalamus also respond to tactile stimulation on the animal's paw (Sans et al., 1970). In the cerebral cortex, vestibular-somatosensory interactions were found in the intraparietal sulcus, and in the animal's primary somatosensory cortex (Schwarz and Fredrickson, 1971; Guldin and Grüsser, 1998; Bremmer et al., 2002). Human neuroimaging studies reported similar convergence (Bottini et al., 1995; Bottini Bottini et al., 2005; Fasold et al., 2008).The parietal cortex also hosts visuo-somatosensory interactions (Bremmer et al., 2002). Finally, trimodal visuo-vestibular-tactile neurons were found in the parietal regions (ventral intraparietal area, VIP; parietoinsular vestibular cortex, PIVC) of non-human primates (although VIP trimodal neurons' tactile responses were for head and face stimulation) (Bremmer et al., 2002; Schlack et al., 2002; Avillac et al., 2007). Area VIP receives, however, a large number of hand and finger projections (Lewis and Van Essen, 2000), although previous multisensory studies of this area emphasised responses to head and face stimulation (Avillac et al., 2007). Interestingly, neurons responding to both visual and vestibular stimulation were reported more frequently than vestibular-tactile cells (Bremmer et al., 2002; Schlack et al., 2002;

Avillac et al., 2007). Nevertheless, integrated visuo-vestibular percepts could clearly influence tactile sensitivity at any of these several levels.

We thus show that the combination of visual and vestibular cues signalling self-motion can significantly influence tactile sensitivity. The anatomical substrate of this interplay is yet to be identified. However, multimodal parietal cortical areas, where all three modalities have extensively been reported to combine, are the most likely candidates. Finally, our results shed some light on the possible functions of the vestibular-tactile interaction reported previously. We found that variations in somatosensory perception were better explained by the influence of a self-motion percept, rather than with 'raw' vestibular signals. This finding is consistent with the possibility that somatosensory enhancement reflects a functional consequence of navigation in the environment, rather than a mere epiphenomenal accident of vestibular cortical wiring.

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Part 3. Vestibular effect on visual attention & awareness

Study 5: Vestibular effects on orienting exogenous and endogenous covert visual attention

Personal contribution: designed research, performed research, analyzed data, wrote the paper.

Vestibular effects on orienting exogenous and endogenous covert visual attention

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Abstract

How do we orient our attention to visual stimuli during movements that displace our head and our whole body? While exogenous (stimulus driven) and endogenous (voluntarily controlled) attention have been extensively explored in static conditions (e.g. Posner, 1980), the impact of vestibular signals, which underlie the coding of space and of the body in space, on visual attention remain underexplored.

Here we used passive whole body rotations as exogenous or endogenous attentional cues to study their effects on orienting visual attention in a classical Posner paradigm. In two experiments we show that - when employed as an exogenous stimulus - rotation impacts attention orienting only at early stimulation latencies. However, when acting as an endogenous stimulus, rotation provides a robust benefit to target detection throughout the stimulation. Implications for attentional and multisensory research are discussed.

Introduction

One key component of attention is the ability of directing its focus towards relevant stimuli in the environment, i.e. action orienting. Attention orienting might be driven automatically, due to the occurrence of an external stimulus capturing attention – exogenous orienting. This has been opposed to endogenous orienting, during which subjects voluntarily orient attention to a new location. In order to study exogenous orienting, Posner and colleagues (Posner, 1980; Posner, Snyder, & Davidson, 1980; Possamaï, 1986) developed a classical paradigm that is characterised by a brief and lateralised flash – the cue – that facilitates the detection of a subsequent stimulus – the target – appearing in the same location and hinders the detection of a stimulus appearing in a different location. In order to study endogenous orienting, a central arrow is presented pointing to either side of space, where on the majority of trials the target will appear. Detection is facilitated for targets appearing on the side where the arrow points to, and hampered for targets appearing on the opposite side (Posner, 1980; Posner et al., 1980; Ristic & Kingstone, 2006).

Original studies on endogenous and exogenous orienting used visual stimuli both as the cue and the target (Posner 1980, Posner et al., 1980). Later on, the finding that a stimulus in one sensory modality (e.g. vision) acted as a cue for a target presented in another sensory modality (e.g. touch) was considered an important demonstration for the existence of crossmodal attentional mechanisms (Driver & Spence, 1998a, 1998b; Macaluso, Frith, & Driver, 2000; Spence & Driver, 2004). Such mechanisms process spatial features of a stimulus independently of the sensory modality in order to direct attention towards a spatial position of increased probability of stimulus occurrence.

In order to orient attention in space, information about the position and direction of the eyes, head and body need to be effectively combined with incoming signals from other senses (i.e. visual and auditory cues) to provide accurate spatial attention and, eventually, motor responses. Important

signals indicating head orientation in the environment come from the vestibular system. Accordingly, there has been an increased interest in recent research as to how vestibular information affects cognitive functioning and attentional processes in particular.

Early insight into the relationship between vestibular function and attention has initially been provided by clinical research with patients suffering from hemispatial neglect, i.e. a deficit in attending to the contralesional side of space usually following right brain damage (Halligan, Marshall, & Wade, 1989). In these patients it has been shown that the degree of the attentional deficit decreases partially after caloric vestibular stimulation (Bottini et al., 2001; Cappa, Sterzi, Vallar, & Bisiach, 1987; Hans-Otto Karnath & Dieterich, 2006; Vallar, Sterzi, Bottini, Cappa, & Rusconi, 1990).

In healthy volunteers several findings support the presence of vestibular effects on attention (Ferrè, Longo, Fiori, & Haggard, 2013; Hartmann, Grabherr, & Mast, 2012; Lewald & Karnath, 2001). Using different attention paradigms (temporal order judgement (TOJ), line bisection, mental number line, sound localisation) and different forms of vestibular stimulation (caloric vestibular stimulation (CVS), galvanic vestibular (GVS), muscle vibration, large-field visual stimulation (background optic flow), physiological vestibular stimulation via a rotating chair/motion platform) these studies converge in showing that vestibular stimulation biases attention orienting to one side of space, in accordance with the stimulation method used (with a few exceptions where no such effect was observed (Rorden, Karnath, & Driver, 2001), or the effect was inconsistent (Shuren, Hartley, & Heilman, 1998)).

Whereas galvanic, caloric, neck-muscle vibrations and other vestibular stimulation techniques do allow stimulation of the vestibular system, they also stimulate many other systems including thermal, tactile, proprioceptive, nociceptive, and other sensory and motor systems (C Lopez, Blanke, & Mast, 2012; Christophe Lopez & Blanke, 2011). Moreover, these techniques do not allow stimulation of

selective afferents of the vestibular system, such as a specific otolith (sensing linear acceleration, e.g. by head motion or gravitational force) or a specific semicircular canal (sensing rotational acceleration around any of the three cardinal axes). Vestibular stimulation provided on human motion platforms allows exposure of human subjects to physiological vestibular stimulation and to stimulate the vestibular organs and their afferent pathways selectively. Using a motion platform, Figliozzi and colleagues (Figliozzi, Guariglia, Silvetti, Siegler, & Doricchi, 2005) found that clockwise (CW) and counter clockwise (CCW) rotations biased the temporal order judgement towards the ipsiversive rotation direction. Thus, it appears that the vestibular signal produced by whole-body acceleration around the yaw axis (earth-vertical axis), stimulating the horizontal canals, acts as an exogenous stimulus, orienting attention in the direction of rotation. However, several important points remain unclear concerning vestibular effects on attention. Namely, whether the orienting effect occurs and is of similar strength throughout the duration of the vestibular stimulus or is only present during specific moments of rotation: for example, at the moment of the strongest discharge of vestibular organs (Goldberg & Fernández, 2000) or at the moment of the discharge onset. More importantly, no previous study raised the question of whether vestibular stimulation may also act as an endogenous stimulus, allowing participants to attend more efficiently e.g. in the direction of stimulation when voluntarily deciding to do so.

Here we set out to investigate whether passive whole body rotations have a robust effect of orienting attention (as measured by the classical Posner task, Posner 1980), and whether they can act effectively as exogenous (Experiment 1) and endogenous (Experiment 2) cues. Participants were asked to indicate whether a visual target (presented at different moments during rotation) appeared to the right or to the left of a central fixation cross while a motion platform accelerated them either in the CW or CCW direction. In Experiment 1 the direction of rotation was tested as an exogenous orienting stimulus (with the chair motion irrelevant to the task); in Experiment 2 we explicitly

instructed participants that the direction of rotation will, in most cases, predict the side of target onset. For both experiments we expected a facilitation in the congruent (rotation side corresponds to stimulus onset side) and inhibitory effects in the incongruent condition (opposite rotation and stimulus onset sides) as compared to a neutral condition where the chair was stationary, thus not providing any orienting cues. We also explored whether the effects would be strongest when the target appeared right after the rotation onset (i.e. 100ms after the beginning of rotation), around peak acceleration (i.e. at 1000ms), or during maximal velocity (i.e. at 2000ms). In this way, we tested whether any vestibular effect on attentional processing were more strongly associated with the initial discharge of the vestibular organs, to their maximum discharge, or to the duration of stimulation.

Materials and Methods

Participants

Fifteen healthy adults naïve to the purpose of the study, with normal or corrected vision and no history of inner ear disease, participated in Experiment 1 (3 females, mean age 27.4 ± 3.6 yr.), and fourteen – in Experiment 2 (4 females; mean age 25 ± 2.8 yr.). All participants gave informed consent and received monetary retribution at 20 CHF/hour. The studies were approved by a local ethics committee and were conducted in accordance with the Declaration of Helsinki.

Experimental setup

The same experimental setup was used for both experiments (Figure 1). The experiments took place in a sound-shielded room in complete darkness. Participants were comfortably restrained by a 5-point racing harness in the chair of a servo-controlled (PCI-7352) rotation platform (±0.1° precise

positioning) (Prsa, Gale, & Blanke, 2012; van Elk & Blanke, 2013). Participants' heads were aligned with their bodies' z axis and positioned at the centre of rotation. Head movements were prevented by using a forehead bar and a chin rest. A 22'' computer display was mounted 40cm in front of the participants. Stimuli were presented on the screen via an on-board computer using custom Python-based software (ExpyVR). Participants used a keyboard to respond. White noise was played to participants through headphones during the experiment to prevent auditory cues.
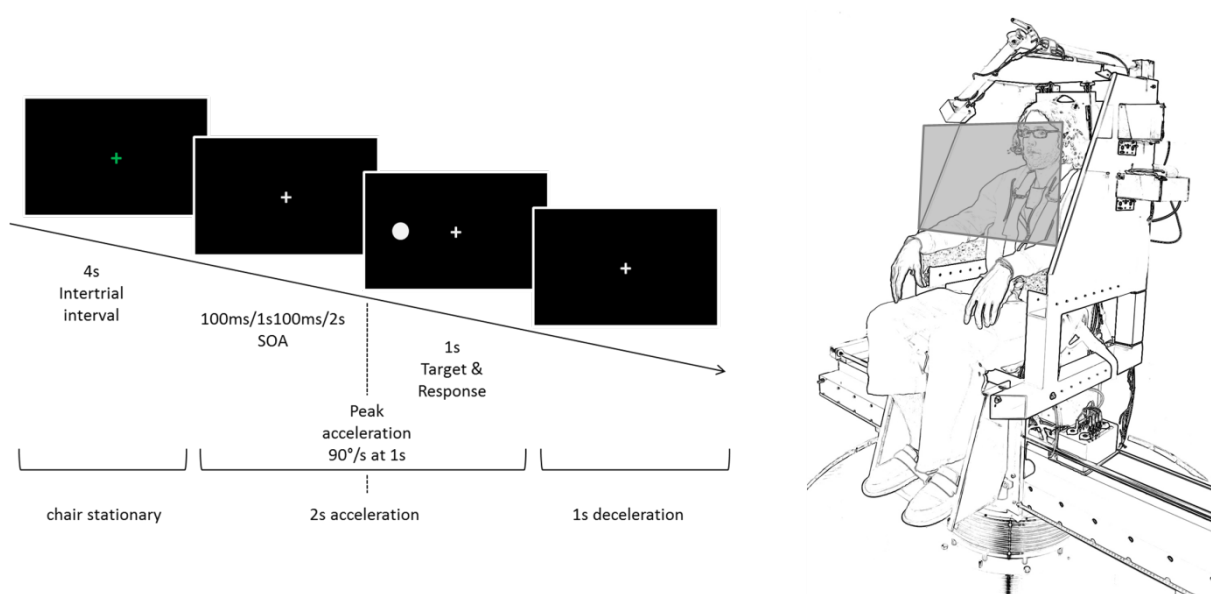
Figure 1. Schematic representation of an experimental trial and the setup for both experiments. Participants were seated in the rotating chair with a monitor in front of them. A grey fixation cross indicated the beginning of a trial. Participants had to indicate as fast as possible whether a grey dot appeared on the right or on the left part of the screen.

Experimental procedure

In both experiments participants performed a Posner task, in which they were asked to respond as fast and as correctly as possible to a grey circle appearing either on the right or on the left side of the screen (see below for details). A central fixation cross was present at all times to minimise eye movements and participants were requested to maintain fixation on it during the trials (Figure 1).

Experiment 1

In Experiment 1 we investigated whether CW or CCW rotations would act as an exogenous attentional cue, affecting the accuracy and the speed of participants' target detection. Performance in stationary trials without any chair rotation was used as a baseline condition (i.e. neutral condition of the classical Posner task). Participants were instructed to respond as fast and as correctly as possible indicating the side where the target appeared. This was done by pressing either the right or the left arrow keys of a keyboard with the index or middle finger of their right hand (i.e. the right arrow was always pressed with the index finger, and the left arrow – with the middle finger). Participants were told that on some trials the chair would move and on others it would remain stationary. They were asked to ignore the chair movements.

The sequence of an experimental trial is represented in Figure 1. A green cross was presented in the centre of the screen. The trial started when the cross turned grey. On rotation trials, the rotation began at the same time as the cross changed colour. The rotating platform accelerated during two seconds and decelerated during one second. Peak acceleration (90°/s) occurred one second after the beginning of rotation (see also (Prsa, Gale, & Blanke, 2012; van Elk & Blanke, 2012). The duration of each trial was 3 seconds. The target was a grey circle (1.5 cm diameter) that appeared at 17° of visual angle either to the left or to the right of the fixation cross. In order to study the temporal relationship between vestibular cue and response modulation, on different trials the target appeared at either 100, 1100 or 2000ms after the beginning of the trial. The target was presented for one second during which the subject responded. When the trial ended the cross turned green again. The inter-trail

interval was of 4 seconds. During the task, participants were requested to keep fixation at the central cross and to try and suppress reflexive eye-movements to the target.

There were 9 experimental conditions: three cue-to-target delays (100, 1100, 2000ms) by three rotation conditions (congruent rotation, incongruent rotation, stationary baseline). The chair rotation conditions were coded with respect to the side of target onset as: congruent (e.g. CCW/CW rotation + target appearing on the left/right part of the screen), incongruent (e.g. CCW/CW rotation + target appearing on the right/left part of the screen) and baseline (no-rotation + right/left side target) conditions. There was the same number of CCW and CW rotations and left and right side targets. Participants performed a total of 574 trials (64 trials per condition, i.e. the number of congruent, incongruent and baseline trials was the same) that were presented in a random order in four blocks (144 trials per block). The whole experiment lasted for about an hour and a half.

Experiment 2

The setup of Experiment 2 was the same as in Experiment 1, except that, crucially, in this experiment the rotation was used to orient attention endogenously. Thus, participants were explicitly instructed that the direction of rotation would on most of the trials predict the side of target onset and were asked to covertly shift their attention in the indicated direction while maintaining fixation of the central cross. Again, they had to respond as fast and as correctly as possible indicating the side on which the target appeared, by button press, as described for Experiment 1.

As in Experiment 1, there were three cue-to-target delays (100, 1000 and 2000ms) occurring in three conditions: congruent, incongruent and baseline. Participants performed a total of 574 trials. Following the classical Posner paradigm the distribution of trials was set so that the rotation predicted the side of target onset in 80% of the cases, thus yielding the following trials combinations: 104 congruent trials, 24 incongruent trials and 64 baseline (no-rotation) trials

Statistical analysis

For both experiments we performed a 3 (cue-to-target delay: 100, 1000, 2000) X 3 (rotation type: congruent, incongruent, no-rotation) ANOVA on both the accuracy and the reaction times values.

Results

Experiment 1: exogenous attention

Reaction times

The 3 by 3 ANOVA run on reaction times (RT) revealed a significant main effect of cue-to-target delay $(F_{(2, 28)}=56.205, p<0.0001)$, of rotation type $(F_{(2, 28)}=69.944, p<0.0001)$ and a significant interaction $(F_{(4, 56)}=9.9871, p<0.0001)$ (Figure 2). Post-hoc Newman-Keuls comparisons performed on the main effects showed that participants were significantly faster when the visual target appeared at 1100ms and 2000ms compared to 100ms (both $p < 0.001$), with no difference between the former two conditions $(p=0.08)$. Participants were also faster in the two rotation conditions (no difference between congruent and incongruent, $p=0.9$) with respect to the no-rotation baseline condition $(p<0.001$ for both).

Post-hoc Newman-Keuls analysis performed on the significant cue-to-target delay * rotation type interaction $(F_{(4, 56)}=9.9871, p<0.0001)$ revealed the following results (Figure 2). First, there was no difference between the congruent and the incongruent conditions for any cue-to-target delays $(p=0.14, 0.75$ and 0.45 respectively). Next, examining how participants' reaction times changed in the three rotation conditions as a function of cue-to-target delay, we found that for both the congruent and the incongruent conditions, participants were significantly faster the later the target appeared (i.e. faster at 1100ms than at 100ms, and even faster at 2000ms) (all $p<0.001$). However, in the no-

rotation baseline condition participants responded equally fast at the two late cue-to-target delays (p=0.93), and at both these delays they were faster with respect to 100ms (both p<0.001).

To refine the analysis and to directly compare the effect of congruent vs. incongruent rotations, we further conducted the same analysis including only the reaction times for the congruent and the incongruent conditions (3*2 ANOVA). There was a significant main effect of cue-to-target delay as reported earlier ($F_{(2, 28)}=47.801$, p<0.0001); and, more importantly, a significant time*rotation interaction ($F_{(2, 28)}=3.5109$, p=0.044). Post-hoc Newman-Keuls analysis showed that participants were significantly faster in the congruent condition than in the incongruent condition, but only at 100ms (p=0.028; at 1100ms p=0.58, and at 2000ms p=0.24).

Finally, we controlled for several biases in the present data. To check for any effects of the finger used to respond (middle or index) we ran a 3 (cue-to-target delay) by 3 (rotation type) by 2 (finger used) ANOVA. No main effect of finger ($F_{(1, 14)}=3.3665$, p=0.09), or interaction of the finger used with other factors was found to be significant. To control for any effect of the direction of rotation we ran a 3-way ANOVA comparing RTs for CW, CCW, and no-rotation conditions ($F_{(2, 28)}=66.093$, p<0.0001). Post-hoc Newman-Keuls comparisons showed no difference between CW and CCW rotations (p=0.89); RTs during CW and CCW rotations were significantly faster than during the no-rotation baseline, in accordance with the above analysis (both p<0.0001).

In conclusion, in Experiment 1 we found that rotation, in either direction, strongly boosted RTs as compared to the baseline condition without rotation and found this at all cue-to-target delays. In addition, in the case of vestibular stimulation, we found a facilitation effect in the congruent condition as compared to the incongruent condition, but only at the shortest cue-to-target delay, i.e. 100ms. Taken together these findings suggest that vestibular inputs are facilitatory attentional cues during a visual attention task, with a direction specific effect only at the short cue to target delay.
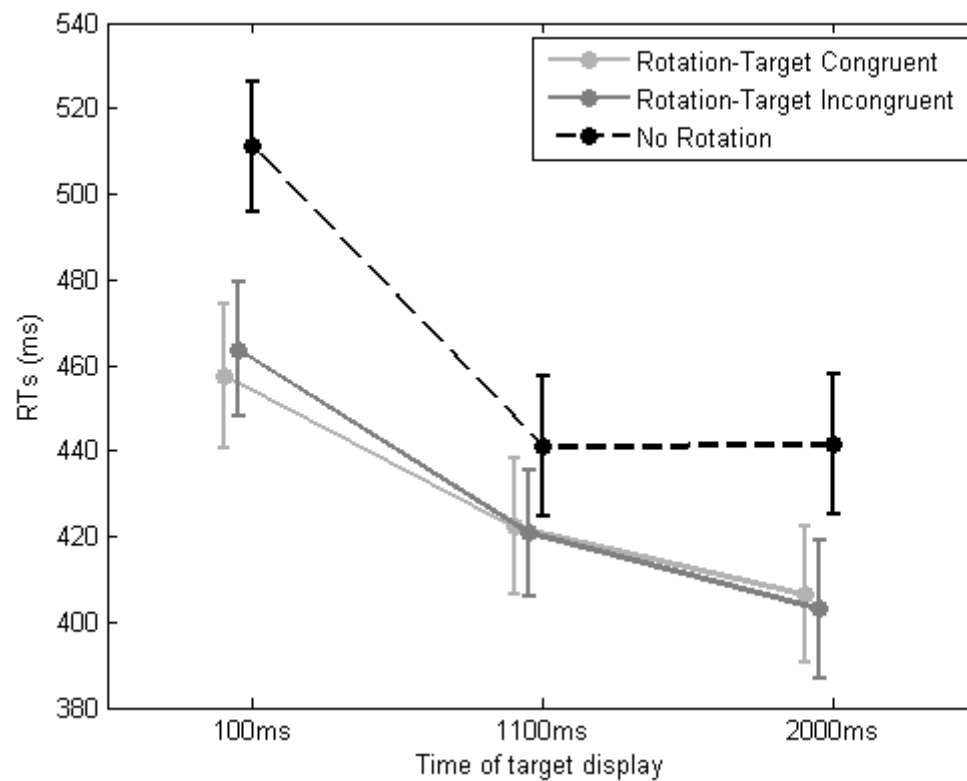
Figure 2. Experiment 1. Mean reaction times and standard errors (shown by error bars) for the congruent, incongruent and the no-rotation condition at the three cue-to-target delays.

Accuracy

Overall participants made very few errors (1.2%). The 3 by 3 ANOVA showed a significant main effect of the cue-to-target delay ($F(2, 28)=4.0837$, $p=0.028$), participants being equally accurate at 1100ms and 2000ms (post-hoc Newman-Keuls comparison, $p=0.58$), and significantly less accurate in the 100ms cue-to-target delay condition ($p=0.04$ and $p=0.02$ respectively). The ANOVA also yielded a significant main effect of rotation ($F(2, 28)=11.718$, $p<0.001$) with participants being equally accurate in the congruent and the incongruent conditions ($p=0.24$), and significantly less accurate in the no-rotation baseline in comparison to the former two (both $p < 0.01$). No interaction was found ($p=0.69$).

Experiment 2: endogenous attention

Reaction times

A 3 by 3 ANOVA (cue-to-target delay * rotation type) revealed the two main effects and the interaction to be significant (cue-to-target delay: $F_{(2, 26)}=22.049$, $p<0.0001$; rotation type: $F_{(2, 26)}=45.309$, $p<0.0001$) (Figure 3). Post-hoc Newman-Keuls comparisons performed on the main effects showed that the later the target appeared the faster participants responded (100ms to 1000ms $p=0.0006$ and 1000ms to 2000ms $p=0.014$). Participants were also significantly faster in the congruent condition as compared to the incongruent and baseline conditions (both $p<0.001$), with no difference between the latter two ($p=0.19$).

The results for the significant cue-to-target delay * rotation interaction ($F_{(4, 52)}=10.111$, $p<0.0001$) are shown in Figure 3. Reaction times in the incongruent and no-rotation baseline condition were not different from each other at 1000 and 2000ms (both $p>0.75$), but participants were faster in the incongruent condition than in the no-rotation baseline condition when the target appeared at 100ms ($p=0.0001$).

Next, we examined how participants' reaction times changed in each of the three rotation conditions as a function of cue-to-target delay. In the congruent condition, RTs became shorter at increasing cue-to-target delays (all p values <0.001). This effect was absent in the incongruent condition, where RTs did not differ depending on the cue-to-target delay (all $p >0.27$). In the no-rotation baseline condition, in keeping with results from Experiment 1, participants were significantly faster when the target appeared at 1000ms and 2000ms compared to 100ms (both $p <0.001$), with no difference between the former two ($p=0.28$).

Finally, we controlled for biases due to rotation direction or response finger. As in Experiment 1, the 3 (cue-to-target delays) by 3 (rotation type) by 2 (finger used) ANOVA failed to show a significant main effect of the finger used ($F_{(1, 12)}=.00319$, $p=0.96$) or any interaction with this factor. The 3-way

ANOVA controlling for the chair rotation direction (CW, CWW, no rotation) was significant (F(2, 26)=53.134, p<0.0001) and the post-hoc Newman-Keuls comparisons showed no difference between CW and CCW rotations (p=0.89), both yielding significantly faster RTs than the no-rotation baseline (both p<0.001).

To sum up, we observe a cueing facilitation effect in the congruent condition, with the effect being progressively stronger at longer cue-to-target delays. There was no detrimental effect in the incongruent condition, as compared to the baseline no-rotation condition.
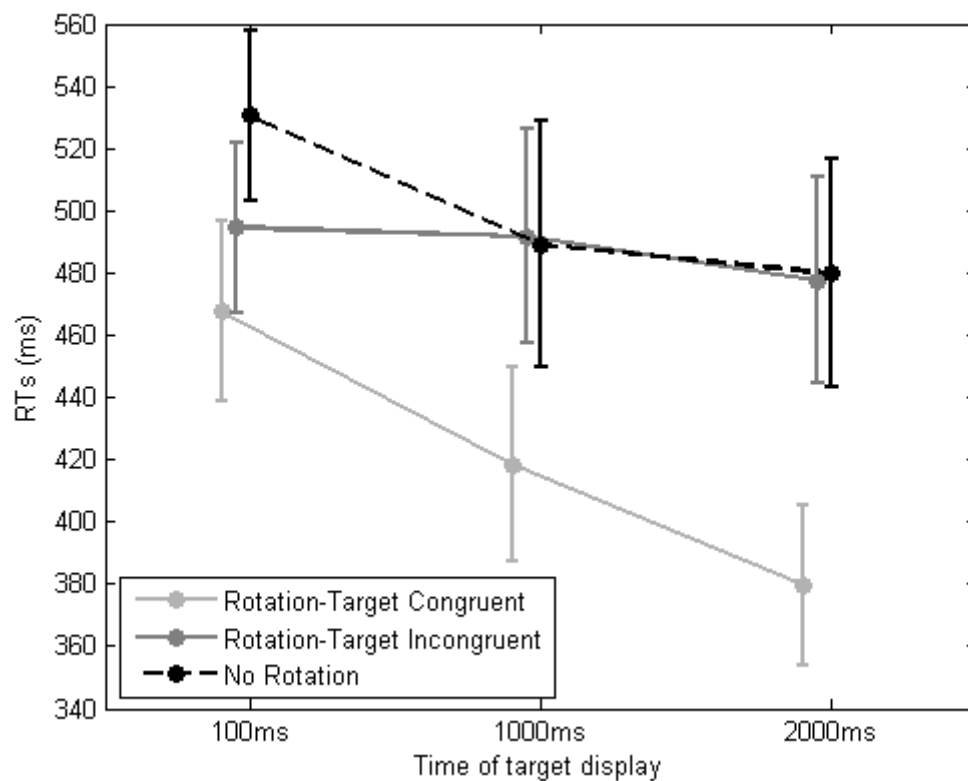
Figure 3. Experiment 2. Mean reaction times and standard error (shown by error bars) for the congruent, incongruent, and the no-rotation condition at the three cue-to-target delays.

Accuracy

Overall participants made few errors (2.6%). A 3 by 3 ANOVA (cue-to-target delay * rotation type) showed no significant differences between experimental conditions.

Discussion

In two experiments we examined how vestibular stimulation in the form of passive whole body yaw rotations modulates attentional orienting. We report three main findings. First, vestibular stimulation leads to behavioural facilitation associated with faster responses in Experiment 1 and 2 and higher accuracy in Experiment 1, as compared to a baseline condition without any rotation. This alerting vestibular effect resulted in faster target detection, independently of whether the rotation direction was congruent or incongruent with the side of target onset. Second, we demonstrate that passive whole body yaw rotations may act as an exogenous cue by orienting attention in the direction of rotation. However, this effect was only found at short cue-to-target delays. Third, in the endogenous experiment (Experiment 2) we found a strong orienting effect present at all tested cue-to-target delays.

Attention allows us to detect events in specific spatial locations, thus enhancing their processing and preparing humans for relevant actions. When turning one's head or being turned in a particular direction, an intuitive prediction would be that one's attention is automatically oriented in that direction. Previous research has found that different forms of vestibular stimulation orient attention in such a way. Karnath and colleagues (H-O Karnath, Fetter, & Dichgans, 1996) showed that ocular exploration was biased to one side of space by both CVS and neck muscle stimulation. Ferrè et al (2013) found GVS to influence the direction of the line bisection bias in a stimulation-dependent way. In addition, background motion of optic flow directs attention to the in-coming field. In line with this prediction in the exogenous attention task (Experiment 1), we found a spatial orienting effect

associated with vestibular stimulation: participants' reaction times being significantly faster in the congruent than in the incongruent condition, selectively, at the earlier cue-to-target delay (100ms). This result indicates that vestibular stimulation signalling rotation facilitates ipsiversive target detection for targets presented during the initial phase of rotation. That is, comparable to previously reported tactile and auditory cue facilitation effects, vestibular cues facilitate the orientation of visual attention in the direction of rotation (crossmodal attention orienting (Driver & Spence, 1998a, 1998b; Macaluso et al., 2000; Spence & Driver, 2004). The magnitude of visuo-vestibular attention orienting we have found (~6ms) is smaller than the effects previously reported in Posner-like paradigms (~10-30ms) (Müller & Rabbitt, 1989; Posner, 1980; Santangelo & Spence, 2008). It has, however, been reported that crossmodal attention-orienting effect may be slightly reduced with respect to unimodal effects (Santangelo, Van der Lubbe, Belardinelli, & Postma, 2006; Spence, 2010), 2010).

We found no visuo-vestibular attention orienting effects for cue-to-target delays longer than 100ms. One explanation could be that when passively and unpredictably displaced, and after having attended in the direction of rotation at its beginning (100ms), it becomes irrelevant for the subject in which direction the motion continues. What is of primary importance is to be alert and respond to any kind of stimulus. And this, despite the fact that the vestibular stimulation is at its maximum at 1100ms (the moment of peak acceleration and thus maximum response of the semi-circular canals). Our results imply that peak acceleration of vestibular stimulation has no effect on attention orienting, whereas onset of rotation has. In addition, former studies on cross-modal attention orienting have shown that the magnitude of the orienting effect depends on the spatial correspondence between the cue and the target stimulus (Prime, McDonald, Green, & Ward, 2008; Spence, 2010). For example, if an auditory cue comes from a more eccentric location than that in which the visual target will appear (although both appear on the same side of space), the facilitation

effect is dampened (Gray, Mohebbi, & Tan, 2009). In our task the duration of the vestibular stimulus might mimic such eccentricity: the longer the rotation, the father away from the initial stimulus location the subject is situated, leading to a reduced relevance of the cue and thus cancelling the facilitation effect.

Finally, there is an interesting difference between the visuo-vestibular Posner task implemented in the present study, and the original visual Posner paradigm. When both the cue and the target stimulus are presented visually, they are both coded in the same retinocentric spatial frame of reference. In the present experiment, instead, the vestibular attentional cue was coded in a head-centred reference frame, while the visual target was coded in a retinocentric reference frame (i.e. the monitor displaying the visual target moved together with the rotating chair). Thus, the present visuo-vestibular orienting effect required remapping of both the cue and the target into a common reference frame or a comparison between the two reference frames. This might also explain why the strength on the cueing effect was lower than in the classical visuo-spatial Posner tasks.

In both Experiment 1 and 2 we also observe an anticipation effect: the later the stimulus appears the faster participants respond. Although on a different time-scale, this effect is also present in earlier work (Green & Woldorff, 2012; Posner, 1980; Posner et al., 1980), where RTs decrease in both congruent (decreasing RTs until about 300ms of cue-target delay) and incongruent conditions (decreasing RTs until about 500ms of cue-target delay). We propose that this effect in the present experiments is due to participants anticipating the target onset when it is not displayed at 100ms. Interestingly, during rotation this effect is present for all the three cue-to-target delays: participants are faster at 1100/1000ms than at 100ms and are even faster at 2000ms (in Experiment 2 the effect is only present for the congruent condition). In the baseline condition where the chair was stationary the effect is only present between the first and second presentation times, there being no additional benefit at 2000ms. We suggest this difference between the rotation conditions and the no-rotation

baseline in Experiment 1, and the congruent condition and the baseline in Experiment 2, is due to the additional temporal information contained in the vestibular stimulus. Indeed, in the no-rotation condition only the change in the colour of the fixation cross (indicating the beginning of a trial) is a cue as to when the target may appear. The rotation of the chair may act as an additional temporal cue, maintaining the anticipation effect. Our paradigm also provides an estimate of the duration of such temporal cueing effects: it is still present 1000/1100ms after the beginning of a trial but provides no further advantage at 2000ms if no additional information is present.

The present data also show, that both congruent and incongruent conditions yield faster responses and fewer errors than the no-rotation baseline condition. We interpret this result as an increase in arousal/vigilance provoked by vestibular stimulation, resulting in increased alertness and general attention to the task. Under this hypothesis, vestibular stimulation would act as a general alerting signal, possibly overriding a more fine-grained directional orienting at later latencies.

In summary, Experiment 1 shows that passive whole body rotations as used in our study have a directionally specific influence on visual attention, but only if visual stimuli are presented shortly after the beginning of rotation. We also observed a general facilitation effect of rotation, likely due to arousal modulation, facilitating target detection during rotation and independently of condition. In contrast to a classical Posner paradigm the no-rotation baseline condition does not allow to infer whether the difference between the congruent and incongruent conditions at 100ms is a result of facilitation due to congruency or impediment due to incongruency of the cue-target relation. That is, usually, in Posner-like tasks, the facilitation effect of exogenous orienting due to cue-target congruency is inferred from faster responses in the congruent condition as compared to a baseline no cue/uninformative cue condition, and, at the same time, the inhibitory effect due to cue-target incongruency is inferred from slower responses in the incongruent condition with respect to baseline (Posner, 1980; Posner et al., 1980). As in our results both the congruent and the incongruent

conditions yielded faster responses than the no-rotation baseline, it remains unclear whether the difference between them is driven by a facilitation effect due to the congruent rotation or by an inhibitory effect due to incongruent rotations.

The results of Experiment 2 show that when explicitly made task-relevant, passive whole-body rotations facilitate target detection in a robust rotation-direction specific way. For all three cue-to-target delays, participants were significantly faster in the congruent as compared to the incongruent and baseline conditions. Our results differ somewhat from classical findings on endogenous attention orienting, however, in that we find no RT or accuracy costs when participants are attending to the uncued location. That is, in our study participants are not slower in the incongruent condition as compared to the no-rotation baseline condition, and sometimes even faster in the former than in the latter (at 100ms). A putative explanation of this result falls into the lines of the facilitation hypothesis we proposed for Experiment 1. Increased alertness during rotation could compensate for a misinformative cue, thus reducing the cost in the incongruent condition. At later latencies the effect of arousal in incongruent trials is further dampened due to enhanced voluntary control, whereas in congruent trials the RTs are shorter (as compared to Experiment 1) due to the voluntary effort.

A recent study by Green and Woldorff (Green & Woldorff, 2012) explored the timing of endogenous attention orienting. In a classical Posner setup under stationary conditions (without any motion of the subjects) their results show that early (≤100ms) orienting effects of an arrow cue are driven by slowing of RTs in the incongruent condition and that participants only benefit from the congruent cue at later stages. Our results show that whole-body rotation provides an orienting benefit even at early stages (100ms), and that this effect is present independently of the incongruent condition. That is, the effect is not driven by slowing down of RTs in the incongruent condition, but by faster RTs in the congruent condition as compared to the baseline (as mentioned earlier, the RTs in the incongruent condition remain the same at every stimulus presentation time). Interestingly, when the

target appeared 100ms after rotation onset, subjects reported (during post-experimental debriefing) that it either preceded the rotation or occurred at the same time as the rotation started. These observations emphasise the fact that despite being consciously perceived as uninformative, rotations maintained an orienting effect (i.e. successfully facilitated target detection). We suggest that this early facilitation effect is due to the fact that at 100ms passive whole-body rotations have an exogenous effect on attention orienting, as we show in Experiment 1. The observed difference between the congruent and incongruent conditions is thus a combined exogenous-endogenous orienting effect (Berger, Henik, & Rafal, 2005).

Our results indicate that vestibular stimulation in the form of passive whole body rotations around the earth-vertical axis is most effective as an attention orienting stimulus at early stimulation latencies and when made task-relevant, as when participants are explicitly instructed to take rotation direction into account. In a sense our endogenous orienting experiment (Experiment 2) mimics voluntary movement whereby one decides to turn and attend in a certain direction, thus providing additional cues for attention orienting.

In conclusion, our experiments show that vestibular stimulation in the form of passive whole body rotations successfully acts as an attention orienting cue. These findings add information with respect to an extensive body of literature on crossmodal attentional effects, by showing that along with auditory, visual and tactile cues, vestibular stimulation orients visual attention exogenously at early cue-to-target delays (Driver & Spence, 1998a, 1998b; Macaluso et al., 2000; Santangelo et al., 2006; Spence, 2010; Spence & Driver, 2004). In addition, the vestibular orienting effects are enhanced when space is made relevant for the task subjects are performing; the facilitation effect due to spatially congruent rotational cues was not only stronger, but also present at all cue-to target delays in the endogenous orienting task.

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Study 6: Balancing awareness: Vestibular signals modulate visual consciousness in the absence of awareness

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Balancing awareness: Vestibular signals modulate visual consciousness in the absence of awareness

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Abstract

The processing of visual and vestibular information is crucial for perceiving self-motion. While visual cues, such as vection, have been shown to induce and alter vestibular and visual percepts, the role of vestibular information in shaping visual awareness is yet unclear. Here we investigated if vestibular signals influence the access to awareness of invisible visual signals. Using vestibular stimulation (passive yaw rotations), and continuous flash suppression (CFS) we tested if congruent visual-vestibular information would break interocular suppression more rapidly than incongruent information. Yaw rotations were applied by means of a motion platform and participants viewed an optic flow stimulus masked using an adopted CFS procedure. The direction of the suppressed optic flow could be congruent (opposite direction as is occurring in natural self-rotation) or incongruent (same direction) with the direction of physical self-rotation. We found that when the unseen optic flow was congruent with the vestibular signals perceptual suppression as quantified with the CFS paradigm was broken more rapidly than when it was incongruent. A control experiment indicated that this was not due to post-perceptual response or detection biases. We argue that vestibular signals impact the formation of visual awareness and our results indicate that multisensory integration of unconscious visual and vestibular signals can affect perceptual experience by causing enhanced access to awareness for congruent multisensory stimulation.

Keywords: Consciousness; Vestibular stimulation, Body Consciousness, Continuous flash suppression, Multisensory integration, Visual awareness

1.   Introduction

Visual and vestibular information are combined in many centers of the brain in order to allow accurate self-motion perception (Berthoz, Pavard, & Young, 1975; F Bremmer, Kubischik, Pekel, Lappe, & Hoffmann, 1999; Siegler, Viaud-Delmon, Israël, & Berthoz, 2000), postural control (Johannes Dichgans & Brandt, 1978; Horak, Shupert, Dietz, & Horstmann, 1994) spatial orientation (Clement, Fraysse, & Deguine, 2009; Ferrè, Longo, Fiori, & Haggard, 2013; Lackner & DiZio, 2005; Villard, Garcia-Moreno, Peter, & Clément, 2005), and have recently also been associated with bodily self-consciousness (Lenggenhager, Smith, & Blanke, 2006; Lopez, Lenggenhager, & Blanke, 2010; Pfeiffer et al., 2013). During self-motion under natural conditions visual and vestibular information are typically congruent, meaning that full-field optic flow on the retina moves in the direction opposite to the movement of the head/body. Behaviorally, it has been shown that such congruent visuo-vestibular cues are integrated and, moreover, that participants are more accurate in judging the amount and direction of self-motion when presented with both visual and vestibular information as compared to only one of these senses (Fetsch, Turner, DeAngelis, & Angelaki, 2009; Kaliuzhna, Prsa, Gale, Lee, & Blanke, *2015;* Prsa, Gale, & Blanke, 2012b). Concerning the involved brain mechanisms, animal studies have demonstrated early visuo-vestibular convergence at the level of the vestibular nuclei (J Dichgans, Schmidt, & Graf, 1973), the thalamus (Lopez & Blanke, 2011; Magnin & Putkonen, 1978) and in several regions within the so-called vestibular cortex (Avillac, Hamed, & Duhamel, 2007; Frank Bremmer, Klam, Duhamel, Ben Hamed, & Graf, 2002; Grüsser, Pause, & Schreiter, 1990).

Moreover, both visual and vestibular cues influence each other when perceiving external objects and self-motion. Indeed, perceived self-motion induced by a rotating visual stimulus is abolished by concurrent vestibular stimulation in a conflicting direction (Young, Dichgans, Murphy, & Brandt, 1973; Zacharias & Young, 1981). On the other hand, visual stimuli bias the perceived direction of self-motion (as administered by a rotational device), and may even reverse it, the perceived motion being the one dictated by vision (Ishida, Fushiki, Nishida, & Watanabe, 2008; Probst, Straube, & Bles, 1985; Wright, DiZio, & Lackner, 2005). In addition vestibular stimulation (in the form of caloric stimulation or passive whole body rotations) has been shown to modulate the perception of bistable visual stimuli (Ngo, Liu, Tilley, Pettigrew, & Miller,

2007; van Elk & Blanke, 2012) and the mental rotation of visually presented bodily stimuli (van Elk & Blanke, 2014). Mental transformation of visually presented stimuli is also affected by damage to the vestibular end organs (Grabherr, Cuffel, Guyot, & Mast, 2011) as well as exposure to microgravity (Grabherr et al., 2007) Finally, visual perception is also affected by the observer's position with respect to gravity (Lobmaier & Mast, 2007; Lopez, Bachofner, Mercier, & Blanke, 2009). Collectively, these studies point towards extensive visuo-vestibular interactions for self-motion and visual perception.

While the integration of visuo-vestibular information for postural control and perception has been extensively studied it is yet unclear whether vestibular information can affect the formation of visual awareness. While early theoretical accounts of consciousness suggested that multisensory integration cannot be achieved without conscious awareness (Baars, 2002), several studies now show that tactile (C. Lunghi, Binda, & Morrone, 2010; Claudia Lunghi, Morrone, & Alais, 2014), olfactory (Zhou, Jiang, He, & Chen, 2010) and proprioceptive (Salomon, Lim, Herbelin, Hesselmann, & Blanke, 2013) information may influence visual awareness. For example, we have recently shown that congruency between one's hand position and the position of a visually presented hand (that is task irrelevant) affects access to visual consciousness (Salomon et al., 2013). This suggests that bodily signals, which are typically not the focus of consciousness, affect the formation of human visual awareness. It also indicates that some level of multisensory integration takes place even in the absence of awareness (Liad Mudrik, Faivre, & Koch, 2014) and has measurable effects on our perception of the world. However, as previous vestibular studies have employed stimuli, which were consciously perceived (e.g. Van Elk and Blanke, 2012) the role of vestibular information in shaping visual consciousness has not been investigated.

Here we tested whether and how vestibular information may impact visual awareness. We employed a variant of the binocular rivalry paradigm called breaking continuous flash suppression (b-CFS) (Jiang, Costello, & He, 2007; Stein, Hebart, & Sterzer, 2011; Tsuchiya & Koch, 2005). This paradigm suppresses a visual target presented to one eye by the rapid presentation of high contrast images ('Mondrians') to the other eye. The time interval for the target to overcome this suppression and the subject report the target is used as the dependent variable. This paradigm has been previously employed in several studies using unimodal visual

stimuli and has shown to bring to light the differences in processing of different types of stimuli such as inverted versus upright bodies (Stein, Sterzer, & Peelen, 2012), familiar words (Jiang et al., 2007) and emotional stimuli (Craig, 2008; Yang, Zald, & Blake, 2007). To provide vestibular signals we used a human motion platform providing natural vestibular stimulation around the yaw axis (passive whole-body rotations). Participants were presented with optic flow stimuli to one eye, which were suppressed by rapid presentations of Mondrian suppressors to the other eye. Critically, the direction of the optic flow and the self-rotation were randomized such that in half the trials the optic flow stimuli were congruent in relation to the expected natural movement of the visual world during rotation (visual stimuli moving in opposite direction to self-motion) and in the other half the optic flow was incongruent with the natural expected rotation (visual stimuli moving in the same direction as self-motion). Thus, in the congruent condition the vestibular information and unconscious visual information are consistent with stimulation occurring under natural self-motion conditions. Participants had to report the color of the dots in the optic flow array, thus both the visual and vestibular rotations were task irrelevant. Following previous results on visual-proprioceptive stimulation during CFS (Salomon et al., 2013), we hypothesized that trials with congruent visual and vestibular information would have shorter suppression times than incongruent trials when optic flow is suppressed by CFS but would show no difference when not visually suppressed (as in the control experiment).

2. Methods

Participants

Participants in the main experiment were 20 right handed healthy volunteers (10 females) from the student population at EPFL (age 19-31 years, $M = 22.7$ years). The control experiment included 19 right handed participants (7 females, age 20-28 years, $M = 23.2$ years). All participants had normal or corrected-to-normal sight and no psychiatric or neurological history. They participated in the study for payment (about 25 CHF). All participants gave informed consent and the study was approved by the ethics committee of EPFL. Two participants in the main experiment were unable to complete the study due to nausea. Two participants in the

control study were removed from the analysis due to low accuracy rates 2.5 *SDs* below the mean. Another participant was not able finish the experiment as he did not break perceptual suppression.

Stimuli and Procedure

Stimuli consisted of high contrast, colorful, dynamic noise patches used as suppressors ("Mondrians") and target stimuli. The target stimuli were optic flow arrays created and presented by in-house software ExpyVR, a custom built multimedia stimuli presentation software developed with Python 2.6 and the Open Graphics Library v.2.2. The optic flow stimuli were linked to the rotating chair so their speed matched that of the current rotation velocity. Optic flow stimuli were of equal luminance and identical apart from their direction of movement (left or right) and their color (green (RGB:10,60,10) or red (RGB:180,10,10). Thus the low level features of the stimuli were identical. The stimuli were viewed via a head mounted display (HMD) VR1280 Immersion Inc., SXGA, 60 deg. Diagonal Field of View, refresh rate 60Hz). Mondrians were rapidly (10Hz) flashed to the participants' dominant eye (visual angle H: 48° V: 36°) and the optic flow was presented simultaneously to the other eye, covering the whole field of view (Figure1 & supplementary movie 1).
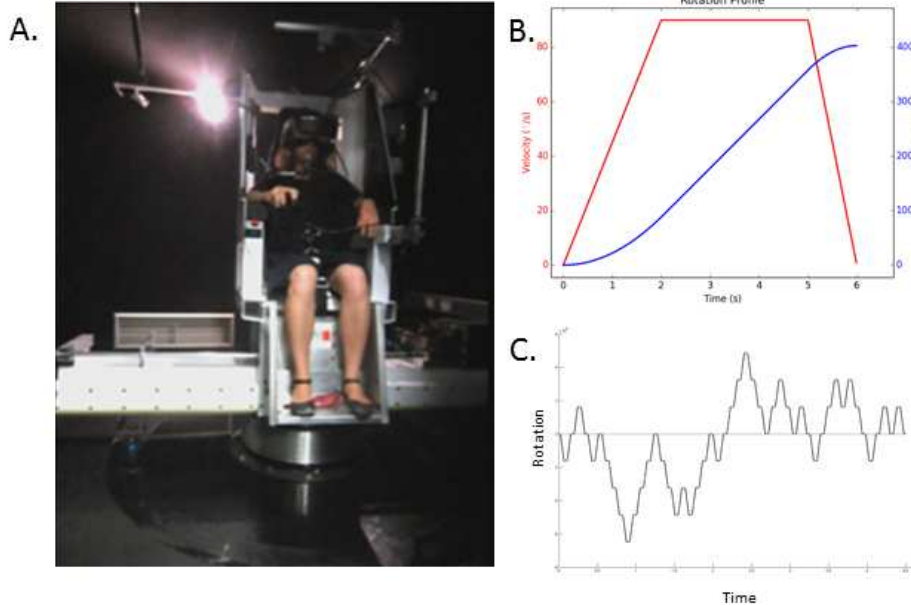
Figure 1. Vestibular platform and stimuli A. Rotating chair platform. B. Angular and velocity profile of rotation for all trials. Note all trials had identical rotation characteristics. C. Example of rotation profile for one block (50 trials). Participants were pseudo randomly rotated around the yaw axis either to the left or the right.

Motion platform

The experiment was conducted in complete darkness in a sound-shielded room in which a motion platform was placed. The chair was mounted on a platform (diameter = 200 cm) fixed on an electrical engine. The electrical engine was digitally servo-controlled (PCI-7352) with precise positioning ($\pm0.01°$). The chair was centered on the rotation axis so that only angular and no linear stimuli were provided to the vestibular organs (Figure1A). Subjects were comfortably restrained with a five-point racing harness, feet straps, and additional cushioning. Images were generated by an onboard computer which was controlled from the outside by network desktop sharing (WIFI). A rumble pad PC game controller (Saitek P2600) was connected to the computer to measure subjects' responses. An infrared surveillance camera was mounted on the chair showing the face of the subjects to the experimenter. Another infrared camera displayed the chair

itself. During the experiment, communication was possible between the subject and the experimenter.

Rotation profile

The chair's rotation profile consisted on each trial of a 2 second acceleration phase to a speed of 90°/s, followed by 3 seconds of constant velocity rotation, and finally, a 1 second deceleration to 0°/s (raised cosine) (Figure 1B). For each block a different rotation profile was generated. The profile varied by randomizing the direction of rotation (Figure1C). The motion platform and rotation profile has been employed in previous work on visual-vestibular, and tactile-vestibular processing (Elisa Raffaella Ferrè, Kaliuzhna, Herbelin, Haggard, & Blanke, 2014; Prsa, Gale, & Blanke, 2012a)

Experimental Procedure

Participants were first tested for ocular dominance using the Miles test (Miles, 1930). During the experiment suppressor stimuli were presented to the dominant eye. Next, to familiarize participants with the visual stimuli they viewed the mask stimuli, as well as both colors of optic flow. Participants were seated on the rotating chair and fitted with the HMD which allowed them to view only the experimental display and not their surroundings. The experimenter then placed their right hand on the response joystick which was placed on their knee. They were instructed to indicate the color of the dots and to respond as quickly as possible when they became visible.

The CFS experiment included 200 trials divided into four blocks. The total duration of the experiment was about one hour. Each trial began with the simultaneous presentation of the Mondrians and target image to separate eyes (See Figure 2 A) and the rotation of the chair in one of the two directions. To avoid an abrupt onset of the target stimuli the contrast of the optic flow was ramped up from zero to full contrast over a period of 2 seconds (Salomon et al., 2013). The trial ended when participants pressed a key on a joystick to indicate their response causing the

screen to become black, or if no response was given until the end of the rotation profile (6 seconds). To assure identical vestibular input for all subjects, rotation was continued even if participants responded. Optic flow color, direction as well as rotation direction were pseudo randomized. We employed a full factorial 2x2 design with factors visual-vestibular congruency (congruent/incongruent) and stimuli color (red/green) (See Figure 2 B).

Following the experiment participants filled in a questionnaire for demographic data and were questioned about the perceived content of the pictures they viewed, what they believed the objective of the experiment was, and whether they felt that their rotation direction affected their performance on the task.

In line with previous studies (L. Mudrik, Breska, Lamy, & Deouell, 2011; Salomon et al., 2013) we employed a control experiment to control for possible differences in detection time due to response or detection criteria. The control experiment was nearly identical to the main experiment with the exception that the optic flow was blended into the Mondrians and presented binocularly. Hence, in the control experiment there was no interocular suppression. Therefore, comparison of the results from the control and CFS experiments could indicate whether detection speed differences are specific to unconscious processing or related to differences due to a response bias or detection thresholds (Jiang et al., 2007).
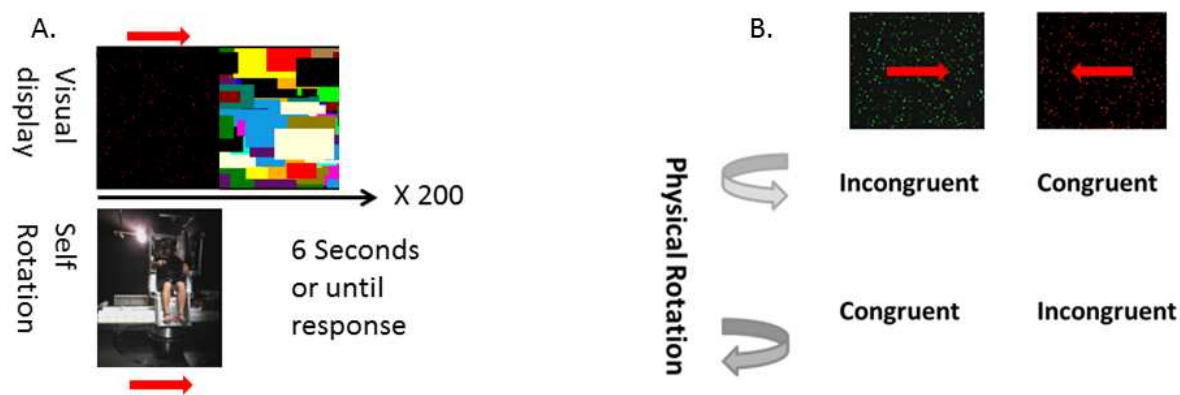
Figure 2. Experimental Design A. Example trial. Participant begins self-rotation and is presented with optic flow and Mondrian suppressors. B. 2x2 experimental design. Optic flow direction in one eye was either congruent or incongruent with participant's self-rotation (e.g.

congruent visual flow opposite to rotation direction as in natural self-rotation and vice versa). Participants were required to indicate the color of the dots in the optic flow array.

Data analysis

Response times (RTs) for erroneous trials and reaction times more than 2.5 standard deviations from the mean (less than 3% of trials) were removed from the analysis. RTs were submitted to a 2x2 repeated measures ANOVA with factors visual-vestibular congruency (Congruent/Incongruent) and direction of rotation (Right/Left). A similar ANOVA was conducted for accuracy rates.

3. Results

Reaction times

The 2x2 ANOVA on the RTs of the correct trials revealed, as predicted, (Figure 3 group average & Figure 4 individual participants) a main effect for visual-vestibular congruency ($F(1, 17)=8.70$, $p=0.008$, $\eta^2=0.33$) Thus, in trials in which the direction of the optic flow and the rotation direction were in opposing directions suppression broke more rapidly ($M = 4.43$ s, $SE = 0.21$) than in the incongruent condition ($M = 4.48$ s, $SE = 0.21$). There was no main effect of rotation direction ($p>0.35$) nor was there a significant interaction between the factors ($p>0.4$).

Control experiment RTs were submitted to an identical 2x2 ANOVA. Unlike the CFS results the control experiment results showed no difference between the congruent ($M = 3.6$ s, $SE = 0.13$) and incongruent ($M = 3.54$ s, $SE = 0.11$) conditions ($F(1,15) =2.79$, $p>0.1$). Again there was no significant effect of rotation direction ($p>0.6$) nor an interaction ($p>0.3$).

A joint analysis of the CFS and control experiments in a repeated measures 2x2 ANOVA with experiment as a between subject factor revealed a significant interaction between

experiment and congruency (F(1, 32) = 8.55, p =0.006, η^2=0.21). Thus, the more rapid breaking of interocular suppression found in the CFS experiment (depicted in Figure 4 left for individual subject data) was not present in the control experiment (depicted in Figure 4 right), thus ruling out response or detection biases. As expected there was also a significant effect of experiment (F(1, 32)=23.65, p=0.00003) with faster reaction times in the control experiment (*M*=3.57, *SE*=0.13) than in the CFS experiment (*M*=4.45, *SE*=0.12). No other results reached significance (all p>0.18).
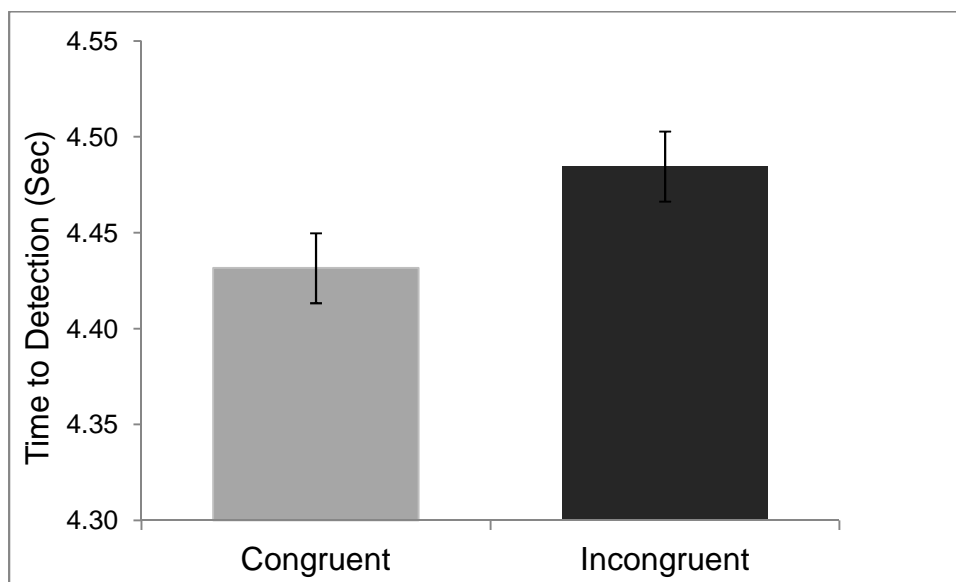
Figure 3. Mean detection time by congruency. Note significantly reduced suppression time when visual-vestibular information is congruent. Error bars are Loftus Masson for repeated measure designs.
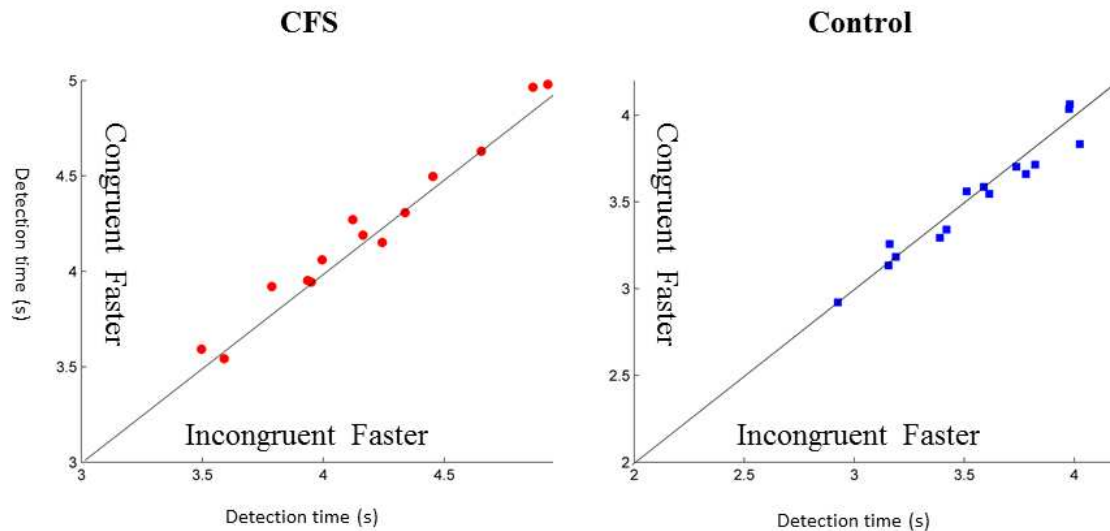
Figure 4. Suppression durations (reaction times) for congruent and incongruent visuo-vestibular stimulations in the CFS experiment (left) and the control experiment (right). Each marking represents the average suppression durations for both conditions for one participant. The line represents the point of equality.

Accuracy

Overall accuracy in the CFS experiment was 89.1%. The 2x2 ANOVA results showed no significant main effects for congruency or movement direction and no interaction (all F<0.7). Overall accuracy in the Control experiment was 86.7%. The ANOVA results showed no main effects for congruency or movement direction and no interaction (all F<0.4).

4. Discussion

The combination of visual and vestibular cues is crucial for self-motion perception and under natural circumstances these two sources of information are necessarily integrated (Fetsch et al., 2009; Prsa et al., 2012b). Our results reveal that visual and vestibular information is integrated in the absence of conscious awareness. Specifically, the data show that when visual motion is suppressed from awareness, concurrent above threshold vestibular information when it is congruent with vestibular information (and comparable to visual motion perceived during self-rotations) will bias visual awareness in the following way. We found that during congruent yaw rotations interocular suppression breaks more rapidly as compared to incongruent vestibular stimulation. This is to the best of our knowledge, the first demonstration that vestibular cues affect access to visual awareness in a psychophysical paradigm. While the integration of consciously perceived visual and vestibular signals has been studied extensively (Fetsch et al., 2009; Lopez et al., 2010; Murray, Wallace, DeAngelis, & Angelaki, 2012; Schlack, Hoffmann, & Bremmer, 2002), our results demonstrate that vestibular signals influence the formation of visual awareness by facilitating access to consciousness for congruent multisensory information. We suggest that this occurs as only the congruent visuo-vestibular condition involves visuo-vestibular integration during natural self-motion.

The finding that visual stimuli congruent with the current self-motion gain faster access to visual consciousness is in line with a large body of evidence in multisensory perception using vestibular and visual cues (Murray et al., 2012; Prsa et al., 2012a). Integration of visual cues signaling self-motion (optic flow) and vestibular cues about self-motion is critical, as under certain conditions information from only one of these modalities is insufficient to accurately judge self-motion (Murray et al., 2012; Probst et al., 1985; Zacharias & Young, 1981). For example, vestibular information is dominant for self-motion perception at high accelerations, whereas visual information is more dominant at low accelerations (Waespe & Henn, 1979). In addition, vestibular organs code for acceleration so without visual cues available perception of self-motion at constant velocities would be heavily impaired. Previous studies have shown optimal

integration for visual and vestibular stimuli moving in opposite directions (Prsa et al. 2012, Fetsch et al., 2010;Kaliuzhna, Prsa, Gale, Lee, & Blanke, 2015). For example in the study of Prsa and colleagues judgments regarding the amount of relative self-motion in two successive rotation were more precise when both visual and vestibular cues were presented together (opposite direction) than when these cues were presented separately. Taken together these studies underline the tight link between these two modalities and their interdependence for visual and self-motion perception.

Whereas these previous studies tested visual and vestibular integration with respect to self-motion and vestibular influences on the processing of consciously perceived visual information, other studies investigated the effects of vestibular stimulation on visual attention (Figliozzi, Guariglia, Silvetti, Siegler, & Doricchi, 2005), bistable visual states, and mental rotation. Of relevance for vestibular input to visual awareness, it was shown by van Elk & Blanke that the direction of passive self-motion influences the perceived rotation direction of bistable rotating stimuli (that under stationary conditions have 50% of chance to be perceived to be rotating in either direction). An upright image of a human body was perceived to be rotating in the same direction as the participant (while looking at the visual stimulus) for a longer period of time than it was perceived to be rotating in the opposite direction (van Elk & Blanke, 2012). These studies highlight the role of vestibular information in affecting visual attention as well as visual awareness for bistable visual stimuli. However, it is important to note that in all earlier studies stimuli were employed that were consciously perceived throughout the task (e.g. visual image of a rotating body/object) and directly task relevant (e.g. judging the order of apparition of two circles). Our study provides, to the best of our knowledge, the first evidence that vestibular information affects visual information processing in the absence of awareness of the visual stimulus. Results from the control experiment allowed us to rule out alternative post perception explanations of these results such as detection or response biases. Importantly, as the visual stimulation was identical in all conditions and a full factorial design was used, the differences found in suppression time must stem from the integration of the vestibular and visual information, rather than any low level features of the stimuli themselves.

The current data extend results from previous studies on crossmodal effects on visual consciousness. For example, a previous CFS study has shown that congruent visual-olfactory stimuli caused shorter suppression times than incongruent visual olfactory stimuli (Zhou et al., 2010). Another study, using CFS has shown that congruent proprioceptive-visual stimuli break suppression faster than incongruent ones (Salomon et al., 2013). Similar effects have been shown for congruent visuo-tactile (Lunghi et al., 2010; Lunghi et al., 2014) and audio-visual stimuli (Alsius & Munhall, 2013). However, to the best of our knowledge, no effects of vestibular information on visual consciousness in the absence of awareness of the visual stimulus have been reported. Taken together, these results suggest than when the brain is faced with a bodily signal of which it is not aware it is more rapid in forming a conscious percept of a congruent visual stimulus. This shows that crossmodal information biases visual consciousness towards the congruent resolution of the binocular visual conflict.

There is a growing body of evidence suggesting that interocular rivalry paradigms such as CFS suppress activity in the visual cortex (Fang & He, 2005; Yuval-Greenberg & Heeger, 2013), suggesting that the formation of visual consciousness is related to activity in primary visual and higher order extrastriate regions (Tong, 2003; Tong, Nakayama, Vaughan, & Kanwisher, 1998). Vestibular stimulation has also been reported to suppress activity in visual cortex (Brandt et al., 2002; Wenzel et al., 1996). Concerning vestibular cortex, previous work revealed visuo-vestibular neural convergence in extrastriate cortex (area MST (F Bremmer et al., 1999; Gu, Watkins, Angelaki, & DeAngelis, 2006), in the parieto-insular vestibular cortex (PIVC (Grüsser et al., 1990; Guldin & Grüsser, 1998)) and in the ventral intraparietal area, VIP (Frank Bremmer et al., 2002; Schlack et al., 2002). Moreover bimodal neurons found in these areas respond to vestibular stimulation and visual optic flow, preferentially in the opposite direction (Avillac et al., 2007; Frank Bremmer et al., 2002; Schlack et al., 2002). Accordingly, we speculate that the present impact of vestibular signals on visual consciousness is mediated through connections between the vestibular cortical system (Guldin and Grüsser, 1998; Lopez and Blanke, 2011) and the visual cortex in parieto-temporal cortex and extrastriate visual regions. This integration of information between sensory modalities and over long cortical distances supports the view of consciousness as resulting from widespread activity across several brain networks (Dehaene &

Naccache, 2001; Tononi & Koch, 2008) and that cerebral representations of self-consciousness (such as self-motion and the related multisensory visual-vestibular cues) impact perceptual consciousness, that is visual consciousness in the present case (Blanke, 2012).

To summarize, our results show that vestibular signals affects the formation of visual consciousness even when they are task irrelevant. This is the first demonstration that vestibular information affects visual consciousness indicating that not only bodily self-consciousness but visual consciousness as well are shaped by multimodal information.

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General Discussion

Summary of the main findings

The vestibular cue occupies a special place among sensory information for several reasons. Vestibular stimulation necessarily produces a multisensory response (Dieterich and Brandt, 2015). Being functionally relevant for several behaviours and through widespread cortical (and subcortical) projections (Lopez and Blanke, 2011), a vestibular stimulus concurrently influences visual (Brandt et al., 1998, Brandt et al., 2002), somatosensory (Bottini et al., 1995, Vallar et al., 1993, Vallar et al., 1990) and proprioceptive cues (Jamali et al., 2014). Interestingly, self-motion (e.g. as employed in the present thesis in the form of passive whole-body rotations), in contrast to commonly employed punctual (i.e. not extended in time) tactile, visual or auditory cues, is extended in time. It is thus an interesting research question, when does vestibular information interact with other cues, and whether the same timing would hold for vestibular-visual as compared, for example, with vestibular-tactile stimuli (both combinations being behaviourally relevant). Finally, although the term "exogenous" has been applied to vestibular stimuli (Figliozzi et al., 2005), a vestibular stimulus can never be truly exogenous, as it signals self-displacement. This is in contrast to other sensory systems encoding motion: visual, tactile and auditory stimuli about motion can be either interpreted as self-motion or motion of the environment. For example, pressure change on the foot soles can be accounted for by a body sway or tilt, but also by the movement of the surface itself (Lenggenhager and Lopez, 2015). In contrast, vestibular information unambiguously indicates active or passive head-motion. All of these characteristics, together with the relevance of vestibular information for navigation (Borel et al., 2008, Péruch et al., 2005), space perception (Ferrè et al., 2013), and the perception of own position in space (Blanke, 2012), make the vestibular sense an important research topic, potentially providing not only answers to conceptual questions in cognitive science but also yielding therapeutic benefits for clinical populations.

The present work has led to the following main findings that have been individually discussed in each corresponding part of the present thesis:

1. Visual and vestibular cues are optimally integrated despite each modality signalling self-rotation around a different axis.
2. Patients with unilateral vestibular loss optimally combine visuo-vestibular self-rotation stimuli.
3. Vestibular stimuli in the form of passive yaw rotation increase tactile sensitivity.
4. Vestibular impact on tactile sensitivity is not direct but is rather a result of a self-motion percept (as provided by a combined visuo-vestibular cue)
5. Vestibular stimulation influences visual attention and especially so, when employed as an endogenous cue
6. Vestibular stimulation impacts visual awareness in a direction-specific way

Below we discuss how these items relate to each other and how they advance the fields of vestibular and multisensory research.

Visuo-vestibular integration

Our work provides further evidence for a strong link between vestibular and visual stimuli. First of all, in line with previous studies, we show that conflicting visual and vestibular cues are integrated into a single self-motion percept (Young et al., 1973, Zacharias and Young, 1981, Probst et al., 1985). Our pilot work, combining visual and vestibular rotation stimuli in differing directions or of different speeds, demonstrates that participants perceive them as a single perceptual event of an intermediate direction and speed. It remains unclear why the same visuo-vestibular stimulus produces different subjective directions of motion across subjects (as described in the introduction, Figure 2). We hypothesise that this result might be due to slight misalignments of the subjects' vestibular organs with respect to the rotation axis of the rotation platform. We have indeed taken care to position the participants so that their heads were tilted forward 30° in order to align the horizontal semi-circular canal with the yaw rotation plane, and have comfortably restrained the participants as well as provided head-fixation by means of a forehead bar and chin rest. However, we cannot entirely exclude that participants could move somewhat during the experiment. We have also seen to it that the screen which provided the visual stimulus was positioned at the same distance for each participant, but it is possible that if participants indeed moved during the experiment, this distance changed, thus producing differences in the angle at which the visual stimulus was delivered. Whether our results reflect such setup inaccuracies or are manifestations of individual sensitivity to visuo-vestibular combinations remains an open question.

In the same vein, other studies also point to some unknowns concerning visuo-vestibular interactions that are of particular relevance to our work. Which cue, the visual or the vestibular, is more dominant for the perception of self-motion? Early studies exploring the interaction of conflicting visuo-vestibular effects have reported contradictory findings about which of the two modalities plays a more important role in the perception of self-motion. For example, Young and colleagues (1973) have shown that when vestibular acceleration (even of a low intensity: $0.2\text{-}1.0°/s^2$) is administered during visually-induced circular vection, vection is disrupted, suggesting a stronger role of vestibular information in the processing of self-motion (Young et al., 1973, Zacharias and Young, 1981). In a similar setup, Probst et al., 1985 used optic flow-induced vection and simultaneously accelerated subjects in the opposite direction (Probst et al., 1985). Subjects had to indicate the perceived onset of self-motion and its direction. Their results demonstrate, contrary to Young et al and Zacharias and Young that the direction of self-motion was always reported as that dictated by visually induced vection.

More recent work on visuo-vestibular integration has also provided different findings. It appears that during passive translational self-motion participants rely more on the vestibular sense (Butler et al., 2010, Fetsch et al., 2009), whereas during passive whole-body rotations the visual cue was found to be dominant (Prsa et al., 2012).

Given the different setups for these experiments, it remains unclear whether the differing findings are related to the protocol used and reflect the actual behaviour, or are due to possible confounds of the stimuli (e.g. difference in the size of the displays delivering visual stimulation, resulting in more or less compelling vection).

In natural settings these two modalities are highly correlated and most often congruent and, as we and others (Butler et al., 2014) show, are integrated even in the presence of strong conflicts between the two cues (**Part 1, Study 1**). As additional evidence for this tight link we also show that unilateral vestibular patients optimally integrate visuo-vestibular cues, and more so on the impaired side, despite the previously reported difficulties in processing unimodal visual and vestibular information (**Study 2**). We also show that visual and vestibular information is integrated before the impact on touch, arguing for early, possibly subcortical interactions between these two modalities (**Part 2, Study 4**).

We would like to take this work a step further and employ the paradigm of visuo-vestibular integration as a diagnostic tool. We are currently conducting exploratory research on visuo-vestibular integration in patients with chronic subjective dizziness (CSD) (Staab, 2012). Previously described as "psychogenic dizziness", this disorder is characterised by non-vertiginous dizziness persisting for more than 3 months and hypersensitivity to own movements and object motion, especially in settings with a dense visual stimulation (as, for instance, in a shopping centre or on an escalator). Patients complain of light- or heavy-headedness, a feeling of imbalance that is frequently not apparent to others, of a feeling that the floor is moving from underneath them, and of a feeling that the ''inside of their head'' is spinning in the absence of any perception of movement of the visual surrounding (Ruckenstein and Staab, 2009). Interestingly, the neuro-otological examination in such patients does not reveal any pathology. This disorder sometimes has psychiatric comorbidity in the form of anxiety and depression (Ödman and Maire, 2008). Treatment of this condition may represent a real challenge, as the aetiology of the condition remains unclear. We hypothesised that CSD patients might have problems in adequately integrating visual and vestibular information which would result in the symptoms described. Using the paradigm described in Study 2 (visuo-vestibular integration in patient with UVL) we are currently testing a cohort of CSD patients (N=15). We have adapted the paradigm in order to test the differential effect of visual noise (number of optic flow dots moving randomly vs dots simulating rotation around a specific axis) on patients' performance. We thus expect to find impaired integration in these patients.

The vestibular sense and multisensory integration of space

Interestingly, our data seem to show integration when one would predict no integration, and no multisensory facilitation when it could be expected. We show that participants optimally integrate visuo-vestibular cues that signal rotation around conflicting axes (**Study 1**). This result is surprising in the light of previous research with visuo-vestibular stimuli but also in other modalities showing that integration breaks down for large conflicts (Ohmi, 1996, Roach et al., 2006). We also show no spatial benefit when participants rotate in the direction of a faint tactile stimulus on either the left or the right hand, tactile sensitivity being similarly increased in congruent (clockwise rotation, right hand stimulus) and incongruent (clockwise rotation, left hand stimulus) conditions (**Study 3**). And finally, when we employed rotations as exogenous stimuli for orienting attention towards a visual target, the effect we obtained was modest and only present at short cue-to-target delays (**Study 5**). Our results might be interesting in the light of recent questioning of the correspondence between the multisensory laws established in animal studies and those evidenced by behavioural work with humans (Spence, 2013).

The field of multisensory integration has rapidly expanded over the last few years lending more and more behavioural support to existing principles of such integration, established based on animal neurophysiology studies. Such studies show that when stimuli from two sensory modalities fall within the receptive field (RF) of a bimodal neuron, multisensory enhancement will be observed (termed the spatial rule) (Calvert et al., 2004, Stein, 2012, Stein et al., 1988). If the receptive field is large, multisensory integration will still be observed even for spatially discordant cues, still falling within this RF. The spatial rule was mostly described for bimodal audio-visual neurons in the superior colliculus of the anesthetised cat. It appears, however, that some behavioural tasks do not yield support for the spatial rule. A recent review (Spence, 2013) reports that tasks on overt and covert attention orienting, as well as those where space is in some way important for the task, multisensory enhancement occurs in accordance with the spatial rule. However, when the task involves a temporal judgement or target identification, multisensory enhancement mostly fails to occur. For example, the perceived intensity of an LED is enhanced by a concurrent auditory stimulus, independently of whether the two originate from the same location or not (Stein et al., 1996). Here the spatial rule would have predicted selective enhancement when the two cues would coincide in space. Other examples also show audio-visual or visuo-tactile facilitation to be space-independent: during a visual temporal order judgement task, tactile or auditory cues preceding the first visual stimulus capture the onset of the light (temporal ventriloquism) and do so even if the two cues are spatially misaligned (Keetels and Vroomen, 2008). Interestingly, there are also studies that yield no support for the spatial rule despite using spatial tasks (Fiebelkorn et al., 2011), and conversely, some evidence (although weak) supporting the spatial rule in non-spatial tasks. For instance Fiebelkorn and colleagues (2011) have shown that the detection of near threshold visual targets is facilitated by concurrent sounds even when the two cues occur with a wide spatial misalignment.

It thus appears that spatial facilitation/enhancement is dependent upon the task the subject is performing. As seen in our attention experiment (**Study 5**), when space and rotation direction are made directly relevant, as in endogenous orienting when the side of target display can be predicted from the rotation direction, there is a pronounced attentional effect. And vice versa: in our visuo-vestibular integration task, the axis around which the vestibular and the visual rotation occurred was irrelevant for the correct performance on the task, as the size of the two rotations was not in conflict.

The absence of an exogenous attention orienting effect for visual stimuli around the peak acceleration appears of interest for elucidating the vestibular effects on tactile processing. We find a general facilitation effect for tactile detection during vestibular stimulation (**Part 2** of the present thesis). This facilitation did not depend on whether rotation was performed in the direction congruent to the stimulated hand, or in the direction opposite to it. We also find that visual attention is not exogenously oriented in the direction of rotation for a target presented around peak acceleration (**Study 5**). The visual target in the attention experiment and the tactile target in the vestibular-tactile experiment occurred approximately at the same time with regards to the peak acceleration time-point. These findings lend further support for the absence of attentional mediation of vestibular facilitation of tactile detection (Bottini et al., 2013, Bottini et al., 2005). In addition, our results in the visuo-vestibular-tactile experiment also show that tactile facilitation during vestibular stimulation cannot be attributed to general arousal due to the vestibular stimulus. Tactile detection is lower during concurrent visuo-vestibular stimulation, whereas an arousal hypothesis would have, on the contrary, predicted facilitation.

Visuo-vestibular-tactile interactions (on-going research)

Building upon our behavioural findings (**Part 2**) we intend to explore the functional mechanisms by which the vestibular stimulation delivered by our platform affects tactile processing, as well as the timing of the visuo-vestibular combination effects. To this aim we are recording somatosensory evoked potentials (SEPs) by left median nerve stimulation during a set of conditions described below. Previous research has shown that CVS affects the N80 SEP component, which has been localised to the parietal operculum – the key region for vestibular processing (Ferrè et al., 2011). We intend to further refine these findings.

The setup of our EEG experiment, directed at exploring effects of vestibular stimulation on tactile processing, is very similar to the experiments described in **Part 2** of the present thesis. Six conditions are being tested (64-channel EEG): 1) a no rotation baseline; 2) vestibular stimulation; 3) visual optic flow in the absence of chair rotation; 4) a combined visuo-vestibular stimulation condition (both cues together in opposite directions). For each of these conditions 500 trials are delivered. Additionally, two conditions without electrical stimulation are recorded: 5) during the no rotation baseline and 6) during vestibular stimulation. 200 trials are tested for each of these conditions. The entire experiment lasts for about 5h.

First, we expect to confirm previous work and other studies conducted in our laboratory. We expect to find vestibular modulation of the SEP components (in the form of suppression) in the vestibular-only condition, as compared to the no-rotation baseline, as, for instance, the suppressed N80 component. We expect no differences between the no-rotation baseline and the optic flow condition. Crucially, due to the fine temporal resolution of the EEG, we would like to explore when the vestibular only condition starts to differ from the combined visuo-vestibular condition. We would expect that early SEP components might be similar between these two conditions, whereas later components would differ, with the visuo-vestibular condition resembling the no-rotation baseline and the optic flow conditions. We will look at evoked potential responses (ERPs) as well as the global field power (GFP) changes.

Open questions

It appears that the timing of vestibular effects on other sensory cues as well as cognition constitutes a delicate issue and is still under question. For instance, we found no exogenous orienting effects in our attention experiment (**Part 3, Study 5**) at late cue-to-target latencies. The present results of the exogenous orienting task do not confirm the findings of Figliozzi et al. (2005) where an ipsiversive attentional shift was found at a much later period – 1500ms. Our setup and procedure differed in several ways from the ones in Figliozzi et al. (2005), however. First, we employed shorter rotations (3 second versus 6 seconds) and the maximal speed our chair reached was of 90°/s as compared to 108°/s achieved in Figliozzi et al. We also had a much shorter interval between trials: 4 seconds versus 15 seconds. Finally, we used a different paradigm to assess attention orienting: Posner task

versus TOJ task in Figliozzi et al. Yet, it is unclear how these parameters would account for the absence of an orienting effect at later latencies in our task. First, the rotations we used were not only consciously detectable but quite strong, thus constituting a salient stimulus. Second, Figliozzi et al. delivered the stimulus 1500ms after the beginning of the rotation. We had comparable times of stimulus delivery: 1100ms and 2000ms. Third, it is possible that during the 4 seconds of the intertrial interval the response of the semi-circular canals did not return to baseline. However, the rotations we delivered would override any such residual activity, inducing a directionally unambiguous and strong vestibular stimulus. Fourth, we note that in their TOJ task Figliozzi et al. administered a total of 36 stimuli (18 synchronous and 18 with varying asynchrony); in contrast, our participants performed 64 trials per experimental condition thus constituting a more reliable dataset. It still might be that stronger accelerations than those used in our task can successfully orient attention in the direction of rotation even at later latencies.

Similarly, it remains an open question whether the vestibular effects we observe using a rotating platform and stimulating the semi-circular canals might differ from potential effects due to the use of a setup stimulating the otolith organs. For example, using a motion platform delivering translational stimuli Hartmann and colleagues (2012) found that leftward and downward displacements facilitated the generation of smaller numbers, whereas rightward and upward displacements facilitated the generation of larger numbers in a random number generation task. This effect was interpreted as due to attentional shifts along the mental number line, showing that here too exogenous vestibular attentional effects have been observed (Hartmann et al., 2012).

It thus appears important to compare translational and rotational stimuli and their effects on other sensory modalities. Previous research in this area is scarce and so far shows, for example, that translational stimuli are processed slower than rotational stimuli, an effect that is thought not to be a result of the dynamics of the sensory organs, but rather to occur at later stages (e.g. during disambiguation of tilt versus translation movement) (Soyka et al., 2013). It would also be of relevance to know the timing of vestibular processing with regards to other senses. GVS stimulation was reported to require a lead of about 160ms in order to be perceived as simultaneous with visual, tactile or auditory stimuli (Barnett-Cowan and Harris, 2009). Whether the same timing would hold for natural vestibular stimulation as well as rotational stimuli remains unclear.

The intensity of the vestibular stimuli necessary to produce an effect on other senses or on cognition also remains unclear. For example, in our vestibular-tactile manipulations (**Part 2, Studies 3 & 4**), a 90°/s velocity was found to increase tactile sensitivity. The threshold, the minimal intensity, of the vestibular stimulus needed for such an effect to occur remains unknown. Would the same intensity hold for translational vs rotational stimuli, and would it have the same magnitude depending on the site of stimulation? (It appears, indeed, that increased tactile sensitivity during vestibular stimulation should be more behaviourally relevant on e.g. foot soles than on the fingertips).

Finally, the distinction between otolith and semi-circular canal involvement in cognition appears highly relevant for self-location and self-identification, as constituents of bodily self-consciousness. The phenomenology of the room-tilt illusion as well as that reported during out-of-body experiences (OBEs) speaks towards an impairment in integrating vestibular otolithic cues. OBEs are accompanied by sensations of elevation and floating (Blanke et al., 2004). Room-tilt illusions can be evoked by the stimulation of the otoliths (Tiliket et al., 1996) and are often reported while moving or driving (Lopez

et al., 2008). It is thus possible that experimental manipulations attempting to induce such experiences would be more successful when performing otolith rather than canal stimulation.

Conclusion

Motion is the most efficient way to interact with the environment. A lot of human cognitive activity takes place during motion, but has mostly been studied in static conditions. Perception, mental imagery, attention orienting, memory retrieval and affective processes all often take place during active or passive self-motion, subtended by a wide vestibular network starting at the vestibular labyrinth and, through the brainstem and thalamus spreading tentacular projections over the cortex. Our work supplements crescent vestibular research by further characterising the multisensory nature of the vestibular sense and its interactions with other senses and cognition. Our findings argue for a strong visuo-vestibular interplay, the two senses being optimally integrated even during overt consciously perceived conflict, and this integration priming on vestibular-tactile effects. We also demonstrate that vestibular stimulation affects visual awareness and attention orienting in ways that on the one hand resemble other multisensory interactions, but, on the other, have idiosyncratic characteristics. We believe future research will provide a fine-grained description of these effects, which would involve characterising the timing of vestibular influence on different senses, the intensity required for the effects to occur, the relation between different types of vestibular stimulation (rotation, translation as well as artificial stimuli), and finally, the anatomical loci of such effects.

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Education

PhD in Cognitive Neuroscience entitled "Balancing the Self", EPFL (started: April, 2011; oral thesis exam: April 22nd, 2015). I am investigating how vestibular information integrates with other bodily signals, such as vision and touch, in healthy subjects and patients with vestibular impairments. My research also concerns the role of vestibular cues for bodily self-consciousness, visual awareness and attention orienting.

September, 2010-March, 2011	Internship in Cognitive Psychology (Universität Bern)
January to August 2010	Internship in Cognitive Neuroscience (EPFL, Lausanne)
September, 2007 – June, 2008	**Master 2** in Neuropsychology (research) **Research topic**: Belief formation and delusions in schizophrenia (Université Pierre Mendès France (Grenoble 2)
September, 2006 – June, 2007	**Master 1** in Cognitive Science (Neuropsychology) **Research topic**: Overcoming perceptual features in logical reasoning, an EEG study (Université Lumière Lyon 2)
September, 2005 – June, 2006	**Master's** degree in Psychology **Research topic**: Mythological elements of an individual's subjective semantics in healthy subjects and patients with schizophrenia (Kiev National Linguistic University)
September, 2001 – June, 2005	**Bachelor's** degree in Philology Speciality: English and Psychology **Research topic**: Psychosemantic and psycholinguistic particularities of modern Ukrainian short stories (Kiev National Linguistic University)

Teaching experience

September, 2013 – August, 2014	Supervision of bachelor student projects (Effects of visual-vestibular rotatory accelerations on covert attentional orienting in touch; Multisensory basis of racial stereotypes) (EPFL, Lausanne)
September, 2010 –	Bachelor degree courses assistant: Physiology-EEG recording; Neuroscience

June, 2013	for Engineers (EPFL, Lausanne)
October, 2011	Class: Depersonalisation Disorder: theory and experimental findings (Universität Bern)
September, 2005 – April, 2006	Bachelor degree classes: Clinical Psychology (Kiev National Linguistic University)

Relevant work experience

May 2014 – October 2014	Co-organising the 2nd VERE PhD Symposium (http://vereproject.eu/) on the science of embodiment and the fusion of the human body with virtual or physical surrogates (Barcelona, Spain)
September, 2008 – December, 2009	Research assistant for behavioural experimentation, EEG recordings & analyses with healthy subjects & psychiatric patients (Institut des Sciences Cognitives, Bron, France)
December, 2004 – April, 2005	Psychologist at a private institution for medical & social rehabilitation (Kiev, Ukraine)
September, 2004 – June 2005	Psychologist at the city clinical psychoneurological hospital (Kiev, Ukraine)

Skills

Software

Matlab, Statistica, SPSS, Elan, EEGLAB, Cartool, E-Prime, ExpyVR, FantaMorph Face Processing Software

Technical skills

Electroencephalography (EEG), Caloric & Galvanic Vestibular Stimulation, Electric Median Nerve Stimulation, 6-Degrees of Freedom Motion Platform, Rotating Platform, Electrocardiogram (ECG)

Languages

Russian, Ukrainian: mother tongues
English, French: full proficiency
German: intermediate
Spanish: conversational

Publications

Published articles

M. Kaliuzhna, M. Prsa, S. Gale, S. Lee and O. Blanke. Learning to integrate contradictory multisensory self-motion cue pairings, in **Journal of Vision**, 15 (1), 2015

M. Bonnefond*, **M. Kaliuzhna***, J.-B. Van Der Henst and W. De Neys. Disabling conditional inferences: An EEG study, in **Neuropsychologia**, vol. 56, p. 255-262, 2014 (*equal contribution)

E. R. Ferre, **M. Kaliuzhna**, B. Herbelin, P. Haggard and O. Blanke. Vestibular-Somatosensory Interactions: Effects of Passive Whole-Body Rotation on Somatosensory Detection, in **Plos One**, vol. 9, num. 1, 2014.

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J. Prado, **M. Kaliuzhna**, A. Cheylus and I. A. Noveck. Overcoming perceptual features in logical reasoning: an event-related potentials study, in **Neuropsychologia**, vol. 46, num. 11, p. 2629-37, 2008.

Submitted manuscripts

R. Salomon*, **M. Kaliuzhna***, B. Herbelin, and O. Blanke. Balancing awareness: Vestibular signals modulate visual consciousness in the absence of awareness (*equal contribution) (Submitted to Biological Psychology)

A. Serino, A-L. Sforza, N. Kanayama, M. van Elk, **M. Kaliuzhna**, B. Herbelin and O. Blanke. Tuning of temporo-occipital activity by frontal oscillations during virtual mirror exposure causes erroneous self-recognition (Submitted to Cerebral Cortex)

M. Kaliuzhna, D. Vibert and O. Blanke. The complex link between bodily illusions, lucid dreams and multisensory integration in a patient with peripheral vestibular damage (Submitted to Multisensory Research, Vestibular cognition, special issue)

M. Kaliuzhna, E. R. Ferrè, B. Herbelin, O. Blanke and P. Haggard. Multisensory effects on tactile detection: visuo-vestibular-tactile trimodal interactions (Submitted to Journal of Neuroscience)

Manuscripts in preparation

M. Kaliuzhna, S. Gale, M. Prsa, R. Maire and O. Blanke. Optimal visuo-vestibular integration for self-motion perception in patients with unilateral vestibular loss

M. Kaliuzhna, A. Serino, S. Berger and O. Blanke. Vestibular effects on orienting exogenous and endogenous covert visual attention

L. Heydrich, **M. Kaliuzhna**, A. Rossetti, O. Blanke and M. Seeck. Ictal postural phantom limb sensation is associated with impaired mental imagery of body parts

Book chapters

M. Kaliuzhna, J-B. Van der Henst. (2014). Le raisonnement et la pensée dans la schizophrénie. Dans N. Franck (Ed.) Cognition sociale et schizophrénie. Elsevier Masson.

Marcel, A., & **Kaliuzhna, M**. (2013). Anosognosia. In H. Pashler (Ed.), *Encyclopedia of the mind.* (Vol. 1, pp. 35-38). Thousand Oaks, CA: SAGE Publications, Inc.

Posters

M. Kaliuzhna, S. Gale, R. Maire, M. Prsa and O. Blanke (2014). Visuo-vestibular self-motion cues are optimally integrated during both clockwise and counter clockwise passive whole body rotations in patients with unilateral peripheral vestibular loss. *XXVIIIth Barany Society Meeting*, *Buenos Aires, Argentina from May 25th - 28th 2014*

M. Kaliuzhna, M. Prsa, S. Gale, S. Lee and O. Blanke (2013). Rotating straight ahead or translating in circles: How we learn to integrate contradictory multisensory self-motion cue pairings. *43d annual meeting of the Society for Neuroscience, San Diego, USA.*

O. Blanke, M. van Elk, S. Berger, C. Pfeiffer, R. Salomon, B. Herbelin, **M. Kaliuzhna** (2013). Vestibular influence on endogenous and exogenous visual attention: A behavioural and ERP study. *43d annual meeting of the Society for Neuroscience, San Diego, USA.*

J. Drury, **M. Kaliuzhna**, H. Guella, A. Cheylus, V. Deprez. (2013) Cross-linguistic interference in French/Arabic bilingual gender agreement processing: ERP evidence. *International Conference on Multilinguism, Montreal, Canada.*

M. Kaliuzhna, B. Herbelin, O. Blanke (2012). Influence of vestibular stimulation on visuo-tactile integration. *42d annual meeting of the Society for Neuroscience, New Orleans, USA.*

M. Kaliuzhna J-B. Van der Henst, V. Chambon (2009). Belief revision in schizophrenia. *17th EPA Congress, Lisbon, Portugal. Abstract in European Psychiatry 24, p. S121*

Oral communications

23.10.2014   2nd VERE PhD Symposium: The complex link between bodily illusions, lucid dreams and multisensory integration in a patient with peripheral vestibular damage. Barcelona, Spain

11.12.2011   Workshop "Feeling of Confidence : Experiments and Current models", ENS, Paris, France