Oscillatory neural responses evoked by natural vestibular stimuli in humans.

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Running Head: Oscillatory response to vestibular stimuli

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Abstract

While there have been numerous studies of the vestibular system in mammals, less is known about the brain mechanisms of vestibular processing in humans. In particular, of the studies that have been carried out in humans over the last 30 years, none have investigated how vestibular stimulation (VS) affects cortical oscillations. Here, we recorded high-density electroencephalography (EEG) in healthy human subjects and a group of bilateral vestibular loss patients (BVPs) undergoing transient and constant velocity passive whole body yaw rotations, focusing our analyses on the modulation of cortical oscillations in response to natural VS. The present approach overcame significant technical challenges associated with combining natural VS with human electrophysiology and reveals that both transient and constant velocity VS are associated with a prominent suppression of alpha power (8-13Hz). Alpha band suppression was localized over bilateral temporo-parietal scalp regions and these alpha modulations were significantly smaller in BVPs. We propose that suppression of oscillations in the alpha band over temporo-parietal scalp regions reflects cortical vestibular processing, potentially comparable with alpha and mu oscillations in the visual and sensorimotor systems respectively, opening the door to the investigation of human cortical processing under various experimental conditions during natural VS.

Keywords: EEG, vestibular processing, vestibular cortex
**Introduction**

The vestibular system encodes three-dimensional displacements of the head and its position relative to gravity. Vestibular signals are used for oculomotor and postural control, but also underpin perceptual and cognitive functions, including visual perception according to internal models of gravity, spatial navigation, and bodily awareness (Brandt et al. 2005; Indovina et al. 2005; Lopez et al. 2010). In strong contrast with the growing number of functions shown to be under vestibular influence is the relative lack of data on the vestibular cortex in animals and humans (Brandt and Dieterich 1999; Angelaki and Cullen 2008; Lopez and Blanke 2011).

Electrophysiological investigations in non-human primates have revealed vestibular responses in several areas of the cortex. These include the intraparietal sulcus, the somatosensory, temporal, frontal and parieto-insular cortices (Schwarz and Fredrickson 1971; Grüsser et al. 1990a, 1990b; Bremmer et al. 2002; Gu et al. 2008; Liu et al. 2011). These areas form a cortical network of which the core is presumed to be located in the ‘parieto-insular vestibular cortex’ (PIVC; Guldin and Grüsser 1998).

Recently, descriptions of vestibular neurons’ spatiotemporal tuning in these cortical regions have been achieved during three-dimensional passive rotations/translations on motion platforms in non-human primates (e.g. Takahashi et al. 2007; Chen et al. 2011; Shinder and Newlands 2014).

Investigations of the human vestibular cortex are challenging because neuroimaging techniques (fMRI, PET) do not allow head and body movements and thus the application of natural vestibular stimulation (VS). Consequently, human
neuroimaging studies have used a variety of artificial VS devoid of physical head motion, such as cold and warm caloric VS, galvanic VS, auditory clicks or short tone bursts (Lopez et al. 2012). These studies revealed vestibular responses in the insular, temporo-parietal, somatosensory, cingulate and frontal cortices (e.g. Bottini et al. 1994; Lobel et al. 1998; Dieterich et al. 2003; Schlindwein et al. 2008). Yet these stimulation techniques activate otolithic and semicircular canal receptors to different degrees, rendering the comparisons between the obtained results difficult. Furthermore, since artificial VS has no physiological equivalent, its use in humans precludes direct comparisons with data about the vestibular cortex in non-human primates collected during natural VS on motion platforms (e.g. Grüsser et al. 1990b; Liu et al. 2011; Chen et al. 2011). While electroencephalography (EEG) has been used extensively to describe visual, somatosensory and auditory cortical responses (Niedermeyer 2005), a detailed description of EEG responses to natural vestibular stimuli and their neural generators is still lacking. Building on prior studies that have attempted to measure vestibular evoked potentials (Hood and Kayan 1985; Pirodda et al. 1987; Elidan et al. 1991; Probst et al. 1995; Constantinescu et al. 1996; Schneider et al. 1996, 2001; Nolan et al. 2009; Nolan et al. 2011; Nolan and Butler et al. 2012; Todd et al. 2014a,b,c; for more detail see discussion), here we report data from a new research platform that allowed us to investigate human cortical processing of natural VS by recording high-density 192-channel EEG while participants underwent passive whole body yaw rotations. We performed two studies (total of four experiments) and analyzed event-related desynchronization of cortical oscillations and vestibular evoked potentials during
transient and constant velocity rotations in healthy participants and a cohort of patients diagnosed with bilateral vestibular loss.
Materials and Methods

Participants.

A total of 22 healthy subjects participated in these experiments: ten healthy subjects (mean age 29.9 ± 3.6 years; 3 women) in study 1 and twelve healthy subjects (mean age 30.4 ± 4.3 years, 3 women) participated in study 2. All healthy subjects were right handed and had normal or corrected to normal vision. Nine patients (mean age 54.7 ± 20; 6 women) diagnosed with bilateral vestibular loss participated in studies 1 and 2. Patients had idiopathic (n=4), ototoxic (n=2), congenital (n=1), ischemic (n=1) or surgically-related (n=1) vestibular loss. The protocol was approved by the ethics research committee at the University of Geneva, and the experiments were performed in accordance with the ethical standards as declared in the Declaration of Helsinki.

Experimental Setup.

Rotational stimuli around the yaw axis were delivered by a custom-built centrifuge chair centered on the axis of rotation (Fig. 1A), therefore providing angular stimulation to the vestibular organs. The chair was digitally servo-controlled (PCI-7352) with precise positioning (±0.1°). Actual displacement kinematics were externally recorded by a triaxial accelerometer (Summit Instruments, 34203A) attached to the chair and positioned directly behind the subjects’ head. Rotation profiles were pre-programmed and specified the chair’s instantaneous angular position at a rate of 100Hz. Constant velocity stimuli were specified manually.
Subjects were restrained in the chair via a 5-point racing harness, with face paddles pressing on the subjects’ cheekbones in order to restrain head movements. Additionally, foot straps and cushioning were used to further reduce subject movement. The rotator was housed in a lightproof and soundproof Faraday cage. White noise was administered to mask auditory cues from the chair during rotation. The vestibulo-ocular reflex (VOR) was suppressed by having subjects fixate straight-ahead on a chair-fixed LED target. We eliminated airflow cues and any residual light reflections emanating from the surroundings by physically enclosing the chair with a dark blanket. Subjects were also monitored throughout the experiment with an infrared camera positioned directly below the fixation target.

Experimental Procedures.

In study 1, we investigated neural responses to transient vestibular stimuli. High-density EEG (see below) was recorded while participants were given a total of 200 rotations (100 rotations in each direction). Healthy subjects had an average of 11±3 trials rejected, while BVPs had an average of 18±10 trials rejected (all figures mean ± standard error). Rotations had a duration of 1.3s following a “raised-cosine” velocity profile (Fig. 1B) (Hood and Kayan 1985; Probst et al. 1995). The peak velocity of the rotation, which occurs at the midway point of the profile (i.e. 650ms) was 110°/s resulting in a total angular displacement of 72°. The angular velocity profile was therefore a single cycle of a 0.77Hz raised cosine function. The inter-stimulus interval separating two consecutive rotations was randomly drawn from a uniform distribution between 1.5s and 2.5s in
order to avoid anticipatory signals. Clockwise (CW) and counterclockwise (CCW) rotations were presented in randomized order in 4 sessions (each lasting less than 3 minutes). The subjects were instructed to stay immobile during each 3-minute session, maintain visual fixation, and avoid blinking of the eyes during rotation intervals.

In study 2, the effects of a constant vestibular stimulus were investigated. We recorded high-density EEG while the participants were rotated at a constant angular velocity of 80°/s for a minimum of 105 seconds (Fig. 1C) in both the CW and CCW direction. Subjects were accelerated to and decelerated from constant velocity in 2s pulses at an average of 40°/s². A shorter post-rotation period, beginning immediately after rotation had stopped, was also recorded. No explicit cues were given to subjects about when rotation would start and end. We also recorded EEG for each participant during a static baseline control condition, without any rotation, for the same length of time. As in study 1, subjects were instructed to remain immobile, maintain fixation, and minimize blinking.

In addition to monitoring subjects throughout the experiments, short breaks were taken between each recording session to control for vigilance and fatigue. Subjects were also given longer breaks where the blanket was removed and the lights turned on.

**EEG Recordings.**

EEG was recorded using a 192-channel pre-amplified scalp electrode system (BioSemi, Inc., Amsterdam, Netherlands) sampled at 2048 Hz and downsampled to 512Hz for analysis. An active reference electrode pair (CMS-DRL) was positioned at the apex of the
skull, and offline analysis was performed with an average reference. Data were transferred for monitoring in real-time to a dedicated recording computer via optical link. Eye movements were recorded by an electro-oculogram (EOG) system composed of four electrodes, placed above and below the right eye and one near each of the left and right lateral canthi.

**EEG Data Analysis.**

*Preprocessing.* Given that whole body rotation inevitably induces VOR, we ensured preprocessing steps were taken to remove the associated artefacts from the recorded EEG. Residual VOR artefacts, as well as other artefacts in our data, were removed from EEG recordings using the FASTER algorithm (Nolan, Whelan, and Reilly 2010), a fully automated statistical thresholding approach to artefact removal in EEG signals. EOG signals were used by the algorithm to remove eye-movement components in the signal related to the VOR. We used the default threshold of three standard deviations from the mean to classify components/channels as artefacts, which FASTER subsequently removed. Channels with detectable artefacts were removed and linearly interpolated from neighboring electrodes for each recording (average of 15 ± 1 out of 192 channels rejected for each subject).

We examined EOG traces before and after artefact removal using FASTER to ensure that eye movements had been removed from our recordings before analysis. Examination of average horizontal and vertical EOG traces of healthy subjects from study 1 aligned with rotation onset before and after preprocessing confirmed that
 artefacts caused by the VOR not successfully suppressed by fixation were either removed or strongly attenuated by FASTER (Fig. 5B).

Study 1: Transient Vestibular Stimulation.

Power spectral analysis. After preprocessing, we computed the power spectral density for each electrode from -0.5s to 2s relative to rotation onset for all trials using the multitaper method (Fieldtrip Matlab toolbox, Mathworks, Natick, Massachusetts, USA). Spectral estimates were calculated for 33 logarithmically scaled frequencies from 1 to 100Hz (i.e. 5 frequencies per octave) and at a 32ms time step. For frequencies above 20Hz, we used a constant smoothing frequency window of 5Hz and a 500ms temporal window yielding 4 multitapers. For frequencies below 20Hz, we applied 2 multitapers using the same temporal window of 500ms and therefore a frequency window of 3Hz. To remove signal components driven by events phase-locked to rotation onset, we first subtracted the evoked potential (i.e. the EEG signal averaged across all trials) from the entire epoch (i.e. -0.5 to 2s relative to rotation onset) of each trial (data were also analyzed without subtracting the evoked potential, yielding nearly identical results). This step was taken as a precaution for data in study 1 only to control for possible extra-vestibular components (Hood and Kayan 1985; Durrant and Furman 1988). The computed time-frequency values therefore correspond only to signals that are not phase-locked. Power was then normalized for all frequency bins with respect to baseline power between -0.5s and -0.1s. The time-frequency method that we used allows for a better visualization of the different natural brain oscillation frequencies whose
bandwidths typically follow a linear progression on a logarithmic scale. Unless otherwise noted, for all spectral analyses power was averaged over all 192 electrodes in order to avoid any possible bias in the choice of electrodes. To compare maximal spectral power during rotation, we averaged spectral power in the same temporal window of interest commencing 650ms after rotation onset (peak velocity) through the end of rotation (1300ms after rotation onset) for both groups (healthy subjects and BVPs). This window contained stimulus peaks in velocity and acceleration and accounted for any potential phase lag between VS and the evoked cortical response (Hood and Kayan 1985; Probst et al. 1995; Grüsser et al. 1990a; Chen et al. 2011). In this manner we compared spectral power in each band, both within and between groups, using the same electrodes (average over all 192 electrodes) and epoch.

**Vestibular-evoked potentials.** We performed an evoked potential analysis on the same transient rotation data of study 1. Data were preprocessed in two ways: 1) with a standard vertex reference and no techniques to remove movement related artefacts (i.e. VOR, movement of EEG cap relative to the skull) and 2) using an average reference and the FASTER algorithm to remove artefacts from the signal. In this manner we were able to compare the results obtained using the same preprocessing as used in previous studies (first preprocessing method used here, as used by Hood and Kayan 1985; Probst et al. 1995) with the results obtained using the present methods (the second preprocessing method). All data were filtered using a zero-phase second-order
Butterworth band-pass filter between 1 and 100 Hz, and a subsequent notch filter at 50 Hz was used to remove line noise. A grand average was then performed on the data.

Study 2: Constant Velocity Vestibular Stimulation.

Power spectral analysis. The firing rates of vestibular afferents from the semicircular canals are proportional to angular velocity but respond to non-zero acceleration stimuli (Goldberg and Fernandez 1971). During a constant velocity rotation, the afferents modulate their activity in response to the initial acceleration pulse as velocity increases from zero to a constant level, and then return to baseline firing rates with a time constant of 5-6s (Büttner and Waespe 1981) despite an ongoing rotation. In the vestibular nuclei, during the first stage of neural processing of vestibular inputs, the time constant of the return to baseline of the stimulus-induced activity is increased (Waespe and Henn 1977), also known as velocity storage. The slow phase of the VOR as well as the reported perception of rotation follow the same dynamics as the activity of vestibular nuclei neurons in response to the acceleration stimulus, both having typical time constants in the 10-30s range (Bertolini et al. 2011). It follows that if we select an “early” period corresponding to the first 5s of constant velocity rotation and a “late” 5s period beginning 100s later (which is between 3 and 10 times the velocity storage time constant), then we can compare the measured cortical oscillations between conditions with and without VS but identical in other aspects (i.e. extra-vestibular sensory cues). Furthermore, this modulation of vestibular activity is also present in the period directly after constant velocity rotation ends (post-rotation); vestibular afferents encode the
deceleration from constant to zero velocity and this activity returns to baseline levels with the same time constant as after the initial rotation onset. We therefore selected the first 5s of rest after rotation offset as the “post-rotation” period, and compared this with average activity during the static condition. The duration of our recordings did not allow for a comparison of early and late post-rotation periods, but note that late and static conditions are equivalent in terms of vestibular activity.

Spectral power was calculated for each electrode during each period (i.e. early, late, post-rotation, etc...) using a Fast Fourier Transform (Matlab, Mathworks, Natick, Massachusetts, USA). A 2s epoch was used for the transform, which was shifted by 1s increments to fill each period (0.5 Hz resolution). Epochs within a period were then averaged to give spectral power for that period. To minimize edge effects of the transform, a Hann window was applied and the linear trend was removed. Relative changes in spectral power (P) at frequency (f) for each electrode (n) were calculated for each subject (s) according to equation 1:

$$P_n(s, f) = 10 \log_{10} \frac{P_{n,\text{test}}(s, f)}{P_{n,\text{base}}(s, f)}$$ (1)

where $P_{n,\text{test}}(s, f)$ is the spectral power during either the first 5 seconds of rotation (early) or post-rotation (post-rotation), and $P_{n,\text{base}}(s, f)$ is the spectral power during either the late period or the average over the entire static condition.

We averaged the spectral power during the test period in the alpha (8-13Hz) band. We also examined spectral power in the beta (14-30Hz) and gamma (30-100Hz, excluding 50 Hz line noise) bands. The logarithm of this power change was calculated so that the data would be approximately normally distributed (Oberman et al. 2005). This
process was also applied to the control condition (static baseline), using the first 5 seconds of the recording as the early period and a 5-second interval beginning 100 seconds later as the late period. As in study 1, spectral power was averaged across all 192 electrodes in order to avoid biases that can be introduced by post-hoc selection of clusters of electrodes.

Topographical analysis.

For descriptive purposes we localized the set of 10 electrodes with the largest magnitude change in each frequency band with respect to baseline for each direction. The sets for each direction were then combined. In this manner we detected whether or not spectral changes in a given band formed a coherent topography on the scalp (clustered) or were sparsely distributed. For study 1, electrodes with the largest power suppression/enhancement were sorted by spectral band during the temporal window of interest. For study 2, electrodes were calculated in each spectral band and for each test versus baseline comparison.

EEG Statistical Analysis

Study 1: Transient Vestibular Stimulation. A bootstrap analysis was used on each electrode to delineate frequency and time bins with power estimates significantly different from their corresponding pre-rotation baseline. To this end, the power estimates for the average of all electrodes were computed 999 times on a different subset of trials by randomly taking for each subset N trials, with replacement, from the
complete set of N trials pooled from all subjects. Bins with significant power changes were deemed to be those that had more than 95% of their bootstrapped estimates that were either greater or smaller than the corresponding pre-stimulus average power (for detailed description see: Prsa et al. 2012). Furthermore, statistical comparisons between band power within the temporal window of interest between groups used a bootstrap test that randomly selected M control subjects or L BVPs, with replacement, from the complete set of M control subjects or L BVPs and compared them as above. Finally, band power at every timepoint was compared between healthy subjects and BVPs by performing a running bootstrap to test for significance. We corrected for multiple comparisons with a cluster-based permutation test of any significant timepoints identified by the running bootstrap results. The labels of healthy subjects and BVPs were randomly shuffled 999 times and the same running bootstrap test was performed on this shuffled data as above, and we recorded the number of consecutive significant timeframes for every permutation. To be considered significant, clusters of consecutive timeframes during rotation in the original dataset had to be larger than 95% of cluster sizes in the permuted dataset.

**Study 2: Constant Velocity Vestibular Stimulation.** We used a cluster-based permutation test (electrode-wise threshold of p < 0.01) to identify contiguous clusters of electrodes that were significantly different when comparing the log spectral power during the test (either the early rotation or post-rotation) periods and baseline (either the late rotation or static baseline) periods, while controlling for multiple comparisons. More specifically,
for each subject we applied a two-tailed t-test at each electrode to the difference in log spectral power between the test period (i.e. early rotation) and baseline epochs. As described in Lenggenhager et al. (2011), we randomly permuted the labels on half of our data for each comparison and then looked for the largest contiguous cluster of significant electrodes in this permuted dataset. This process was repeated for each way of choosing half of the participants within a group (i.e. healthy subjects and BVPs), resulting in a distribution of maximum cluster sizes. Only those clusters larger than 99% of permuted max cluster sizes passed our test (for a detailed description see: Lenggenhager et al. 2011).

**EEG Source Localization.**

The sLORETA software package (Pascual-Marqui 2002) was used for estimating the cortical neural generators for spectral modulations in each band (alpha, beta, gamma) of the EEG scalp recordings (as in Lenggenhager et al. 2011; Evans and Blanke 2012). Neural generators were computed from scalp potentials by using the pseudo-inverse of the electrical lead field, which was derived from a head model based on the MNI152 template (Fuchs et al. 2002). EEG recordings were preprocessed in the same manner as for scalp-level analysis, using the FASTER algorithm to remove artefacts. The subject-wise cross-spectra were first calculated at every electrode for each spectral band, and an inverse transformation matrix (signal to noise regularization of 1) was applied to each cross-spectra. Statistical comparisons within a spectral band and between conditions were carried out at the voxel level using an F-ratio of the log-transformed data (type I
errors were corrected as per Nichols & Holmes 2002). We set our F-ratio threshold for significant voxels to be 1.3 (-1.3 ≥ F ≥ 1.3).
Results

Study 1- Transient Vestibular Stimulation.

Analysis of EEG responses to transient VS in healthy subjects and BVPs focused on relative changes in spectral power during the rotation period as compared to the pre-rotation baseline. This analysis revealed prominent suppression in the alpha and beta bands and enhancement in gamma band.

Alpha Band. Alpha band power was significantly suppressed in healthy subjects: time-frequency bins in the alpha band were significantly suppressed compared to pre-rotation baseline for both CW and CCW displacements (bootstrap test, p<0.05; Fig. 2A). This suppression (averaged across all scalp electrodes) started after rotation onset and reached maximum suppression 1054ms (CW: 1086±79ms, CCW: 1022±63ms) after rotation onset. Alpha band had the largest modulation in spectral power in healthy subjects with respect to other frequency bands when averaged within the pre-selected temporal window of interest, i.e. 650ms to 1300ms (CW=-1.96 ± 0.45dB, CCW=-2.15 ± 0.52dB (mean ± S.E.M.); Fig. 2A). Electrodes with the highest magnitude of alpha power suppression in the time window from 650 to 1300ms were clustered around the vertex over bi-parietal scalp regions (Fig. 2B). Comparing CW and CCW alpha power showed no lateralization of the effect, indicating there was no directional tuning of the observed alpha suppression (Fig. 2B).

In BVPs, alpha band power averaged across all electrodes was also significantly suppressed in time bins during rotation (bootstrap test, p<0.05; Fig. 3A).
Alpha power suppression in BVPs started after rotation onset and reached maximum suppression 1182ms (CW: 1086±111ms, CCW: 1277±268ms) after rotation onset. Alpha power averaged over the temporal window of interest was also suppressed in BVPs (CW=-1.13±0.24dB, CCW=-1.13±0.24dB; Fig. 3A). Electrodes with maximal suppression during this window were not clustered in BVPs, but rather were scattered over parietal, occipital, and frontal scalp regions (Fig. 3B). As in healthy subjects, comparing CW and CCW alpha band power in BVPs showed no lateralization of the observed suppression (Fig. 3B). Although alpha band oscillations were also significantly suppressed in the patient group compared to pre-rotation baseline, the alpha suppression during the temporal window of interest was significantly smaller in the BVPs compared to healthy subjects (CW: p=0.05, CCW: p=0.04; average over all electrodes). A running bootstrap test comparing alpha band power during rotation in healthy subjects to BVPs at every timeframe revealed that alpha power suppression was significantly greater in healthy subjects (bootstrap test, p<0.05; cluster-permutation test, p<0.05) from 764 ms (CW: 797ms, CCW: 732ms) to 1358ms (CW: 1502ms, CCW: 1213ms; Fig. 4B), and thus for a duration of 594ms (CW: 705ms, CCW: 481ms). The power density profile during the temporal window of interest showed a broader pattern of alpha power suppression extending into adjacent lower and higher frequencies as compared to healthy subjects in whom we found a distinct alpha peak (Insets of Fig. 2A (healthy), Fig. 3A (BVPs), and Fig. 4A(difference between healthy and BVP)).
Beta Band. Beta band power was also significantly suppressed during rotation in healthy subjects (bootstrap test, p<0.05; Fig. 2A). Beta power suppression started after rotation onset and reached maximum suppression at 910ms (CW: 1022±141ms, CCW: 797±190ms). Beta power in healthy subjects averaged across all electrodes within the temporal window of interest was suppressed with respect to baseline (CW=-0.41±0.20dB, CCW=-0.49±0.16dB). Electrodes with the largest suppression were clustered around the vertex in bi-parietal scalp regions (Fig. 2C). Comparing CW and CCW rotation showed no lateralization of beta suppression (Fig. 2C). The pattern of suppression we observed for the beta band was primarily at the lower end of the beta range (dark blue shading in Fig. 2A, close to the alpha band frequency range) and was weaker or absent in the higher beta range.

In BVPs, time-frequency bins in the beta band (averaged across all electrodes) were also significantly suppressed during rotation (bootstrap test, p<0.05; Fig. 3A). Beta power suppression in BVPs started immediately after rotation onset and reached maximum suppression 893ms (CW:988±108ms, CCW:797±206ms; Fig. 3A) after rotation onset. BVP beta power during the temporal window of interest was suppressed (averaged across all electrodes: CW=-0.82±0.19dB, CCW=-0.77±0.20dB). Importantly, beta suppression in the temporal window of interest did not differ significantly from that found in healthy subjects (CW: p=0.08, CCW: p=0.14) and scalp electrodes with maximal beta suppression in the BVPs were clustered in the same region as in healthy subjects (bi-parietal electrodes: Figs. 2C and 3C). Again, there was no lateralization of beta suppression when comparing CW and CCW rotations (Fig. 3C). Comparing beta
band suppression between healthy subjects and BVPs at every time point during rotation showed beta suppression was significantly greater in BVPs compared to healthy subjects near rotation onset (bootstrap test, p<0.05; cluster-based permutation test, p<0.05), becoming significantly different between 62ms (CW: 94ms, CCW: 29ms) to 734ms (CW: 831ms, CCW: 637ms; Fig. 4C), for a duration of 672ms (CW: 737ms, CCW: 608ms). Thus, a significant difference between healthy subjects and BVPs vanishes near peak velocity (650 ms), where the subcortical vestibular response is maximal (Fig. 4C).

**Gamma Band.** Power in the gamma band (>30Hz) was significantly enhanced relative to baseline in both CW and CCW directions in healthy subjects (bootstrap test, p<0.05; Fig. 2A). Scalp distributions of gamma power in healthy subjects (averaged during rotation) differed from those of the alpha and beta bands and revealed that maximal gamma enhancement was centered on fronto-polar electrodes (between the left and right lateral recti) (Fig. 5A). The location of these gamma oscillations suggests that they reflect quick phases of ocular nystagmus induced by whole body rotations. The observed posterior local maxima that are apparent in the CW and CCW scalp topographies are characteristic of neural responses to microsaccades measured by EEG (Yuval-Greenberg et al. 2008; Yuval-Greenberg et al. 2009). Despite the implemented controls for ocular artifacts (i.e. visual fixation and EEG artifact removal), residual microsaccades (i.e. quick phases of the VOR) remained (Fig. 5B) and seem to be responsible for the observed gamma band modulations.
In BVPs, time-frequency bins in the low gamma range were significantly suppressed relative to baseline, in contrast to the enhancement found in healthy subjects (bootstrap test, p<0.05; Fig. 3A). This is consistent with the absence of vestibular driven oculomotor reflexes in these patients.

**Theta Band.** Spectral power in the theta band (4-7Hz) was significantly enhanced relative to baseline immediately after rotation onset in healthy patients (Fig. 2A), however this enhancement returned to baseline well before peak velocity (i.e. 650ms). The same pattern of theta band enhancement was seen in BVPs, although there were no time-frequency bins different from baseline during rotation (Fig. 3A). Importantly, theta power did not differ between healthy subjects and BVPs at any time point during rotation, suggesting that enhancement in this band was not vestibular in origin.

**Summary – Study 1**

In summary, the data from study 1 show that yaw rotation is associated with a significant suppression of alpha power over a large bi-parietal scalp region that peaks approximately 350ms after peak velocity (1000ms after rotation onset). Comparisons between healthy subjects and BVPs demonstrated that this alpha modulation lacked a clear topography in BVPs, was significantly smaller in amplitude during the temporal window of interest, and was associated with a less focal power density profile. Beta suppression did not significantly differ between healthy subjects and BVPs during the temporal window of interest, peaked at a similar latency as the alpha suppression, and
had the same scalp topography in both subject groups. Beta oscillations differed at rotation onset, but this effect vanished by peak stimulus velocity. Beta oscillations were also suppressed more strongly in BVPs, while having a similar distribution of scalp electrodes in both healthy subjects and BVPs. This suggests that they reflect extra-vestibular brain processes. Based on the topography and previous EEG findings (Yuval-Greenberg et al. 2008), we presume that significant gamma band enhancement in healthy subjects (and suppression in BVPs) was most likely generated by residual VOR and microsaccades (see discussion). We note that the same analyses were repeated without removing phase-locked components with results that were nearly identical to those reported. Thus, these EEG data in healthy subjects and BVPs suggest that alpha oscillations reflect VS caused by yaw rotation (Fig. 4A). To further investigate the vestibular nature of alpha oscillations we next used a constant velocity rotation protocol.

**Study 2- Constant Velocity Vestibular Stimulation**

We next studied cortical oscillations during constant velocity rotational VS. We examined spectral modulations during the early period of rotation (the first 5 seconds of constant velocity rotation, immediately after the acceleration pulse) when the vestibular response is maximal, and compared these to two different baseline conditions: 1) the late period of rotation from 100s to 105s after constant velocity had been reached; and 2) an average during the static recording (which compares rotation to static as in the transient profile of study 1). Spectral modulations during the post-rotation period were similarly examined; we compared the first 5 seconds of rest after
rotation with the average of the static baseline condition. As with transient stimulation (study 1), constant velocity experiments were performed in both healthy subjects and BVPs.

*Alpha Band.* For healthy subjects, alpha band power was significantly suppressed during the early period compared to the late period for both CW and CCW rotations (Fig. 6A). We performed a statistical analysis over the entire sensor array, using a cluster-based permutation test to control for multiple comparisons ($p < 0.01$ electrode-wise threshold). This test identified a large cluster of electrodes exhibiting alpha suppression over fronto-parietal regions (Table 1; Fig. 6B). Alpha band suppression (averaged across all electrodes) in healthy subjects had a similar topography to that obtained in the prior group of healthy subjects subjected to transient rotations (Table 1; compare Fig. 6A and Fig. 2B). Electrodes with maximal alpha suppression when comparing early and late rotation were clustered in parietal scalp regions around the vertex in healthy subjects (Fig. 6B). The static condition control analysis, in which no rotational stimulus was delivered, did not reveal any electrode that showed a significant difference between the same two periods. Additional analysis confirmed these findings by showing that the difference between early and late alpha suppression during rotation was significantly greater than during the static condition (CW: $p=0$, CCW: $p=0.01$, bootstrap test; Fig. 6C). When analyzing the effects of direction of rotation, no significant electrodes were found based on a comparison of the early periods of CW versus CCW rotation in healthy subjects, indicating there was no lateralization of alpha suppression. Importantly, no
electrodes were found to be significantly different when comparing the late period of rotation with the static baseline indicating that alpha power returned to static levels by the end of constant velocity stimulation. These results demonstrate that alpha band suppression found during rotation in healthy subjects did not result from rotation-related artefacts.

We repeated the same analysis using the average power during the entire static, non-rotation recording, as a baseline. We compared alpha band power in the early and late rotation periods with alpha band power during rest, and thereby matching the extra-vestibular conditions of the transient rotation protocol of study 1. Furthermore, we compared alpha power during the post-rotation period, when subjects were at rest but the vestibular response was maximal, to the same static baseline. Results for both of these cases were similar to those for the early versus late analysis in terms of cluster size, topography, and amplitude for the average across all electrodes (see Table 1).

Alpha suppression was different in BVPs than in healthy subjects. In BVPs, alpha band power was not significantly suppressed (cluster-permutation test, $p>0.01$) at any electrode when comparing early versus late rotation in each direction (average across all electrodes, Table 1; Fig. 7A). No significant clusters were found using the cluster-based permutation test even with a more liberal ($p < 0.05$) electrode-wise threshold (Fig. 7B). In addition, electrodes showing the largest suppression were scattered over the entire scalp for BVPs, differing from the vertex-clustered topography observed for healthy subjects (Fig. 7A). Moreover, early rotation versus late rotation alpha band suppression in BVPs did not differ significantly from early-static versus late-static alpha suppression
during the static control condition, when no VS was given (CW: p=0.34, CCW: p=0.08) (Fig. 7C). Early rotation versus late rotation alpha band suppression averaged across all electrodes in the BVPs was significantly smaller than that found in healthy subjects (CW: p=0.01, CCW: p≈0, bootstrap test; Fig. 8A).

We repeated the same analysis of the patient data but with the average alpha power of the static recording as a baseline. Results comparing the early rotation period and post-rotation period to the static baseline condition were similar to the early versus late analysis in BVPs in terms of cluster size, topography, and amplitude across all electrodes (see Table 1). Note that the relatively few significant electrodes identified in the CW rotation condition were distributed at the outer edges of the montage in several small clusters, as opposed to the single, large fronto-parietal clusters found in healthy subjects.

**Beta Band.** In healthy subjects, clusters of electrodes exhibiting significant beta suppression were found in medial fronto-parietal scalp regions (Table 1; Fig. 6E). Electrodes with maximal suppression were clustered near the vertex in the CCW direction and distributed more frontally in the CW direction (Fig. 6D and 5E). Control analysis of the static condition found no significant electrodes when comparing beta suppression in the early static versus late static periods. Early versus late beta suppression was found to be significantly greater during rotation compared to the static condition, but only in the CW direction (CCW: p=0.15, CW: p=0.03, bootstrap test; Fig. 6F).
When the analysis was repeated for early rotation and post-rotation periods using average beta power during the static condition as a baseline, similar results were obtained in terms of cluster size, topography, and amplitude across all electrodes (see Table 1). However, electrodes with maximal beta suppression were not spatially clustered in these cases, being widely scattered over the scalp for both rotation directions.

For the BVPs, there were no significant clusters (we found 2 electrodes during CW rotation over the left temporal region that were significantly suppressed and survived the cluster-based permutation test) (Fig. 7E) when comparing beta power for early versus late rotation (Table 1; Fig. 7D). Electrodes with the largest beta suppression were clustered in left-frontal regions for CCW rotation and in right-frontal regions in response to CW rotation. Early-rotation versus late-rotation beta suppression did not differ significantly from static-early versus static-late spectral power (CW: p=0.08, CCW: p=0.27, bootstrap test; Fig. 7F). There was no significant difference in early rotation versus late rotation beta band suppression between healthy subjects and BVPs (Table 1; Fig. 8B).

Comparing the early and post-rotation periods to the average of the entire static condition in BVPs again revealed similar results to the above early versus late comparison in terms of number of electrodes exhibiting a significant effect and mean amplitude across all electrodes (see Table 1). However, in these cases electrodes with maximal beta suppression were not clustered.
**Gamma Band.** There were no significant clusters found in the gamma band (one significant electrode in the BVPs that survived the cluster-based permutation test when comparing early-rotation versus late-rotation in the CCW direction). There were no significant spectral modulations in the gamma band in healthy subjects or BVPs for either direction of rotation (two tailed t-test, \(p<0.01\); permutation test, \(p<0.01\)).

**EEG Source Localization (study 2)**

Our findings in study 2 reveal a prominent modulation of alpha-band oscillations in healthy subjects during passive whole body yaw rotations. To further analyze the origin of alpha suppression we localized the neural generators of these changes for each of the comparison conditions (early rotation versus late rotation, early rotation versus static and post-rotation versus static) using sLORETA at the voxel level (see Methods). This was done for healthy subjects and for BVPs. In healthy subjects, comparisons localized the generators of alpha suppression to bilateral parietal cortex, which was centered in Brodmann areas 5 and 7 and extended more posteriorly and laterally towards parieto-occipital and temporo-occipital cortex (Fig. 9; see Table 2). The negative F-ratios in these clusters correspond to alpha suppression of the test condition. Additionally, application of sLORETA revealed smaller volume (<10% of supra-threshold voxels) enhanced activation (positive F-ratios) over right fronto-temporal regions during rotation (centered in Brodmann areas 44 and 22; Fig. 9; see Table 2). This enhancement was not
present for the post-rotation versus static comparison. No significant voxels were found for the BVPs, consistent with results at the scalp level.

Summary – Study 2

As with transient stimulation, the alpha band exhibited the most prominent and consistent modulation in spectral power compared to all other bands in healthy subjects. Moreover, this effect was absent in BVPs. Alpha suppression was significantly greater in healthy subjects than in the BVPs. Beta suppression was weaker and did not differ between healthy subjects and BVPs. There were no statistically significant modulations in either group in the gamma band during constant velocity stimulation.

Evoked Potential Analysis of Transient Vestibular Stimulation.

We performed two parallel analyses of the evoked potentials during transient VS, in order to compare the results obtained using different pre-processing methods. First we performed the analysis using the same preprocessing method employed in previous vestibular evoked potential studies (i.e. a remote reference in lieu of an average reference, and without removing artefacts with the FASTER algorithm; Hood and Kayan 1985; Durrant and Furman 1988; Eildan et al. 1991; Probst et al. 1995). We examined the evoked response at electrode Cz (vertex), as this electrode was reported to have the largest response in previous studies. The evoked response of BVPs and healthy subjects exhibited a similar time course. Both healthy subjects and BVPs exhibited the same previously reported long latency response that lasted the duration of rotation (Fig. 10A).
We found three distinct positive evoked potential components: 1) one commencing at rotation onset and peaking between 40ms and 200ms, 2) one near peak velocity at 650ms, 3) and one at the end of rotation. Comparison with the acceleration profile (grey line in Fig. 10A) demonstrated that these peaks coincided with a zero-crossing, and hence direction change, of stimulus acceleration. This effect was found in both groups and in response to rotation in both directions.

We then repeated the analysis after performing additional pre-processing (average reference, artefact suppression using the FASTER algorithm; see methods), and found that the previously-observed long-latency effect was abolished (Fig. 10B). In healthy subjects, the evoked response consisted of an initial negative peak (CW: 100ms, CCW: 47ms), followed by a positive peak 100ms later (CW: 184ms, CCW: 166ms), and culminating with a negative peak roughly 150ms later (CW: 301ms, CCW: 303ms). We note that as with the first preprocessing method the evoked response in BVPs again had a similar time course to that in healthy subjects. An initial negative peak (CW: 117ms, CCW: 49ms), was followed by a positive peak roughly 100ms later (CW: 201ms, CCW: 180ms), and culminating with a negative peak roughly 150ms later (CW: 328ms, CCW: 328ms). Statistical analysis comparing the healthy subject and BVP response did not reveal any extended periods of significant difference between these cohorts during rotation (bootstrap test, p<0.05 sample-wise threshold; cluster-based permutation test, p<0.05; 100ms temporal threshold). This differs from statistical comparisons of alpha and beta band spectral powers in study 1, which showed long duration (>500ms) significant differences when comparing healthy subject to BVP spectral power.
Discussion

Transient and constant velocity vestibular stimulation

During transient VS subjects were continuously accelerated and therefore semicircular canal afferents were continuously stimulated. This reliably evoked a change in alpha band power, which was suppressed throughout the VS relative to pre-rotation baseline. Importantly, in BVPs this alpha suppression was significantly smaller in magnitude, had no consistent topography and was more diffuse across frequencies. In healthy subjects the alpha band also exhibited the most prominent and consistent modulation in spectral power compared to all other frequency bands. The temporal evolution further linked alpha suppression to the yaw rotation profile: significant alpha suppression occurred after stimulus onset, was maximal after peak velocity, and started to return to baseline levels after rotation ended, somewhat comparable to phase shifts (Grüsser et al. 1990a) and latencies between neural responses in PIVC and VS (Chen et al. 2011).

The use of a constant velocity VS allowed us to examine whether alpha suppression with similar spectral, topographical, and functional characteristics as described for transient VS is also present for constant velocity VS. Comparing the early and late phases of rotation, and additionally the post-rotation with rest periods, allowed us to examine periods with and without vestibular activation but with identical extra-vestibular cues. This is relevant for excluding the contribution of somatosensory signals such as tactile and proprioceptive signals (see below for eye movements), which are inherent to body rotations and present during transient VS, but not during constant velocity VS (we do not discuss interoceptive signals related to VS; i.e. Vaitl et al. 2002).
Accordingly, we argue that the significantly stronger alpha suppression (early vs. late; early vs. rest) in healthy subjects is a correlate of cortical vestibular processing. This finding is strengthened (and extends to different constant extra-vestibular cues present during rotation; Chaudhuri et al. 2013) by the analogous results we obtained during the post-rotation period, after constant velocity rotation had ended, and in which subjects were immobile but the vestibular system was activated. Alpha suppression had the same spectral, topographical, and functional characteristics as during rotation.

Despite motion profile differences, the spectral changes were consistently limited to the alpha band and consistently localized to bilateral temporo-parietal scalp regions. Testing BVPs with the same experimental conditions provides additional arguments that the electrophysiological responses are of vestibular origin. Patients were diagnosed as BVPs based on neuro-otological testing (caloric vestibular stimulation, pendular test, head impulse test) revealed an absence of physiological and perceptual response to VS. In two cases the vestibular pathway to the cortex was fully severed (due to operation); however, we cannot exclude that some minor vestibular input to cortical processing remained in the rest of the patient cohort, compatible with the minor alpha suppression in BVPs. Thus, comparisons between healthy subjects and BVPs in both motion profiles showed that alpha modulation had no consistent topography in BVPs, was absent or significantly weaker in amplitude during the temporal window of interest and associated with a broader power density profile. We adopted the same procedures as previous studies aimed at showing that BVPs have weaker or absent vestibularevoked myogenic potentials (Watson and Colebatch 1998) or deficits in perception and
spatial cognition (Brandt et al. 2005). We cannot fully rule out the possibility that age-related differences between healthy subjects and BVPs may have contributed to the present differences in alpha power between both cohorts. However, while alpha band power has been shown in some cases to change depending on age in terms of magnitude and frequency (i.e. Klimesh 1999), these changes have not been consistent across studies (Duffy et al. 1984, 1993; Pollock et al. 1990), and were much smaller than those reported here. Moreover, age-related changes have also been observed for beta power (Duffy et al. 1993); and yet we found no differences in beta power between groups in the present data, which one would expect if age had been a factor.

Our approach is based on several previous electrophysiological studies in humans. Earlier EEG studies of the human vestibular system were limited in that only 1 to 20 scalp electrodes were used (Hood and Kayan 1985; Probst et al. 1995; Durrant and Furman 1988; Elidan et al. 1991). The majority of these studies demonstrated a long latency vestibular EP, described as a dome-shaped negativity, that was reported to match the rotation profile and to persist for the duration of the stimulus (Hood and Kayan 1985; Probst et al. 1995). Hood and Kayan (1985) used raised-cosine rotational stimuli and measured full-scalp EEG in a group of healthy subjects and BVPs and reported vestibular EP characterized by a negativity (maximal at Cz) that peaked halfway through the rotation profile (at peak velocity) for both groups. This was confirmed by Probst et al. (1995) using a similar VS protocol across different axes of rotations. The present vestibular EP analysis also yielded long latency vestibular EPs consistent with those reported above when signals were referenced to the vertex, with large magnitude
negative peaks in response to changes in direction of the acceleration profile. However, these components were absent when recordings were preprocessed (i.e. re-referencing to an average reference and removal of eye movement). High-density 192 electrode recordings and analysis was further improved by independent component analysis, (Nolan, Whelan, and Reilly 2010; Gwinn et al. 2011), which allowed us to minimize VOR and movement related artefacts. Yet, despite these technical improvements, potentials evoked by transient VS did not differ significantly between healthy subjects and BVPs, indicating that the evoked potential may originate from extra-vestibular sources. By focusing on the analysis of cortical oscillations, our approach overcame the significant technical hurdles of previous electrophysiological investigations of the human vestibular system (Hood and Kayan 1985; Probst et al. 1995; Durrant and Furman 1988; Elidan et al. 1991). Compared to previous EEG work in BVPs, we also performed a group analysis with statistical comparisons between healthy subjects and BVPs that were lacking in previous studies (Hood and Kayan 1985; Durrant and Furman 1988; Elidan et al. 1991). Importantly, in our experiments spectral changes across all studies were only seen (and significantly different between healthy subjects and BVPs) in the alpha band, and not in the beta or gamma frequency ranges. During both transient VS and constant velocity VS beta suppression did not significantly differ between healthy subjects and BVPs, and had the same scalp topography in both subject groups.

However, gamma activity did differ between patients and healthy subjects during transient VS suggesting that it either reflects vestibular activation or alternatively the VOR which is driven by vestibular stimulation and might provoke changes in EEG
gamma power originating from the eye muscles (Yuval-Greenberg et al. 2008, 2009).

Based on the scalp topography and previous EEG findings (Yuval-Greenberg et al. 2008, 2009), we argue that the observed gamma band enhancement in healthy subjects (and suppression in BVPs) was most likely associated with the quick-phase of rotatory and post-rotatory VOR (high-frequency components of eye movements and blinks are not removed by the FASTER algorithm). Controlling the VOR was central to our experimental design and preprocessing steps. First, we asked subjects to fixate in order to suppress the VOR. Second, analytically removing EOG components effectively eliminated the major eye movement artefacts from the EEG data. Third, previous EEG studies investigating the influence and topography of eye movements on electrophysiological studies in humans (Yuval-Greenberg et al. 2008, 2009) reported gamma enhancement as a consequence of microsaccades that gave rise to the same fronto-occipital EEG topography that we observed for gamma enhancement. Fourth, despite different VS profiles (and differences in the resulting VOR) for the transient and constant velocity studies, results in the alpha band were highly consistent across studies, whereas results in the gamma band were not. In conclusion, we argue that the spectral, amplitude, temporal, and topographical findings suggest comprehensively that the bilateral temporo-parietal alpha suppression pattern reflects activation of the thalamo-cortical vestibular system during yaw rotation, whereas the gamma band enhancement reflects residual eye movements.
8-13 Hz alpha suppression over posterior and occipital scalp regions has been linked to visual stimulation reflecting activation of the visual thalamo-cortical system (Berger 1929; Pfurtscheller et al. 1996; Hari et al. 1997). Prominent 8-13 Hz mu suppression over fronto-parietal scalp regions is traditionally associated with activation of the motor and somatosensory cortex (Gastaut 1952; Niedermeyer 2005; Pineda 2005), and both (posterior and sensorimotor) regions have been shown to harbour vestibular representations (Kahane et al. 2003; for review: Lopez and Blanke 2011). We argue that the present alpha suppression is a distinct pattern that reflects activation of the multisensory vestibular cortex in bilateral temporo-parietal scalp regions. The sources of this vestibular alpha suppression are in line with the temporo-parietal vestibular cortex previously identified (Lobel et al. 1998; Bense et al. 2001; Dieterich et al. 2003; Kahane et al. 2003; Hewett et al. 2011; Lopez and Blanke 2011). Future work should distinguish how the present vestibular alpha oscillations compare to alpha oscillations over parietal regions previously linked to attentional (Sauseng et al. 2005; Romei et al. 2008; Haegens et al. 2011; Haegens et al. 2012) and related processes (i.e. Figliozzi et al. 2005; Ferrè et al. 2014). Unlike studies of visual and somatosensory attention that showed a lateralization of alpha suppression (Haegens et al. 2011; Haegens et al. 2012), we note that there was no significant difference between alpha suppression when comparing the early periods of CW and CCW rotation in Study 2, and no lateralized topographies across all studies (Fig. 2B and 3B).

The investigation of human vestibular cortex with non-invasive approaches has proven to be technically challenging. Accordingly, high-density EEG investigations seem
particularlly appropriate to better understand the function, neurophysiology, and location of the human cortical responses during natural VS. Functional neuroimaging studies have used caloric and galvanic VS as well as auditory clicks and short tone bursts to activate vestibular receptors (Lopez et al. 2012; zu Eulenburg et al. 2012). A limitation of these previous approaches is that artificial methods of stimulating vestibular receptors also strongly activate other sensory systems (caloric and galvanic VS activate the tactile, thermoreceptive and nociceptive systems; clicks and short tone bursts activate auditory pathways). Without appropriate controls to exclude extra-vestibular contributions to the activations reported in these studies, it is difficult to establish the exact location and sensory processing in human vestibular cortex.

Linking vestibular processing to alpha band oscillations provides new insights into the human vestibular system and vestibular cortex. The study of cortical rhythms is particularly appropriate to investigating the vestibular cortex, which encompasses a distributed network of multisensory brain areas (Guldin and Grüsser 1998). Although the contribution of vestibular signals to the modulation of cortical oscillations has not been studied in depth, EEG recordings during space flights (Cheron et al. 2006) revealed alpha/mu enhancement over posterior and sensorimotor scalp regions. Additionally, studies in rats showed that vestibular signals contribute to hippocampal theta oscillations (related to the animal’s position in space; Russell et al. 2006; Huxter et al. 2003). Moreover, vestibular signals project to numerous thalamic nuclei and relay and process sensory signals important for cortico-cortical communication and sensorimotor processing (Alitto and Usrey 2003; Sherman 2005). This is compatible with the proposal
that the 8–13 Hz rhythm is a major neural indicator for sensorimotor integration and
“the subject’s relationship to the environment” (Hari 2006) and that it is selectively
suppressed by a variety of sensorimotor and multisensory tasks (Klimesch 1999;
Muthukumaraswamy et al. 2004; Pineda 2005; Del Percio et al. 2007; Babiloni et al.
2008). These different functions all closely relate to primary vestibular functions such as
Accordingly, we propose that alpha suppression in temporo-parietal scalp regions during
yaw rotation reflects cortical processing of vestibular signals in vestibular cortex.


Todd NP, Paillard AC, Kluk K, Whittle E, Colebatch JG. Source analysis of short and long latency vestibular-evoked potentials (VsEPs) produced by left vs. right ear air-conducted 500 Hz tone pips. Hear Res; 312:91-102, 2014c.


<table>
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<th>Table 1. Results for EEG analysis during constant velocity VS.</th>
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Table 1. Results for EEG analysis during constant velocity VS. Results for all groups (healthy subjects and BVPs), directions (CW and CCW), and experimental comparisons for the alpha and beta bands for study 2. Cluster size refers to the size of cluster that survived our cluster-permutation test (p<0.01), common refers to the number of electrodes that were significant in both directions, and spectral power the average spectral power in dB for that comparison averaged over all 192 electrodes. P-value is the result of the bootstrap test comparing spectral power between healthy subjects and BVPs.
Table 2. Supra-threshold voxel clusters from inverse solution of constant velocity VS conditions.

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<td><strong>Early vs. Late</strong></td>
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<td><strong>Early vs. Static</strong></td>
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<td>CW</td>
<td>4</td>
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<td>CCW</td>
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<td><strong>Post vs. Static</strong></td>
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<tr>
<td>CW</td>
<td>9</td>
<td>-54</td>
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<td>CCW</td>
<td>23</td>
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Geographic centers (MNI coordinates) of supra-threshold voxels (F ≥ 1.3) for clusters in each comparison made in study 2. Suppression refers to a lower spectral power in the test case versus baseline, enhancement a higher spectral power in the test case.
Figure Captions

Figure 1. Velocity profiles of vestibular stimulation (VS) delivered by a centrifuge chair.

A, Picture of the centrifuge chair, which was housed in a lightproof and soundproof Faraday cage. B, Raised-cosine velocity profile of 1.3s transient VS protocol used in study 1. Baseline and rotation periods are indicated. “Rot. ON/OFF” refers to intervals when the chair was rotating (“ON”) or immobile (“OFF”), “Vest. ON/OFF” to periods when the vestibular system was actively encoding VS (“ON”) or at baseline activity (“OFF”). C, Velocity profile for constant velocity VS as used in study 2. “Early” and “late” periods are 5s periods when the vestibular system was activated by the rotational stimulus (early) and when it had habituated and returned to baseline levels (late). “Post-rotation” is the first 5s after the rotational stimulus has ended, when rotation had stopped but the vestibular system was actively encoding the deceleration.

Figure 2. Spectral analysis of healthy subjects during transient VS. A, Time-frequency plot for the -0.5 to 2s period relative to counterclockwise rotation onset. Distinct clusters of significant modulation (bootstrap test, p<0.05; white dotted contours) of the averaged response (all subjects and 192 electrodes) were found spanning each frequency band of interest; the most prominent spectral suppression (dark blue shading) was in the alpha and beta bands. Inset shows average spectral power across all frequencies (from 650ms after rotation onset until the end of rotation; see methods for further detail). Rotation onset and offset are indicated with black dotted lines. Spectral power at each frequency bin was first normalized to pre-rotation (-0.5 to -0.1s) levels. B,
Scalp map (192 electrodes) comparing average alpha band power during the temporal window of interest. Blue represents spectral suppression, red spectral enhancement. The topography of the ten electrodes with the maximal effect (shaded region on scalp map, max electrodes) are also shown, as is the scalp map comparing CW and CCW rotation (labeled lateralization). C, Scalp maps comparing average beta band power during the temporal window of interest, corresponding topography of maximum effect, and lateralization.

Figure 3. Spectral analysis of bilateral vestibular patients (BVPs) during transient VS. A, Time-frequency plot for the -0.5 to 2s period relative to counterclockwise rotation onset. One large cluster of suppression (bootstrap test, p<0.05; white dotted contour) of the averaged response (all BVPs and 192 electrodes) was found spanning the alpha and beta bands. Inset shows average spectral power during the temporal window of interest. Scalp maps of all 192 electrodes, topography of electrodes with maximal effect, and lateralization for B, alpha band power and C, beta band power during the temporal window of interest are also shown.

Figure 4. Spectral power difference between healthy subjects and BVPs during transient VS. A, Difference plot between healthy subject and BVP spectral power. Time-frequency bins in which spectral power in healthy subjects is more suppressed than BVPs are shaded in blue. Red/yellow shading indicates spectral power is more suppressed than BVPs in that time-frequency bin. Note prominent alpha suppression. B,
Alpha band suppression during transient VS in healthy subjects (blue line) and BVPs (red line). Green ticks indicate significantly different time-points between healthy subjects and BVPs (bootstrap test, p<0.05; cluster-permutation test, p<0.05). Grey line is the velocity profile. C, The same plot for the beta band.

Figure 5. Gamma band enhancement and grand average EOG recordings from healthy subjects during transient VS. A. Scalp maps of spectral power in the gamma band in healthy subjects in response to CCW rotation. Note the local maxima in fronto-polar and posterior electrodes. B. Grand average of the EOG response in healthy subjects in response to CCW rotation. Raw EOG is shown in grey, EOG that has undergone data processing is shown in black (processed).

Figure 6. Spectral analysis of healthy subjects during constant velocity VS. A, Scalp map of early (first 5s of constant velocity rotation) alpha band power compared to late (5s period commencing 100s later) in response to counterclockwise rotation. Alpha band suppression predominates in posterior scalp regions (blue shading corresponds to spectral suppression). B, Scalp map of p-values showing significant electrodes when comparing early and late alpha band power (two tailed t-test, p<0.01; cluster-permutation test, p<0.01). Shaded regions represent significant differences (blue/white: suppression; red/black: enhancement), un-shaded grey regions electrodes with a p-value>0.01. Topography of max electrodes is also shown. C, Early alpha band power normalized to late period for counterclockwise rotation (black bar) and static baseline.
(grey bar)(mean ± S.E.M.) for the average of all electrodes. Early alpha band power was significantly suppressed compared to late power during yaw rotation but not for two similar periods during static baseline condition. Suppression during rotation was significantly greater than modulation during the static case (bootstrap test, p=0.01). D, E, F Same analysis as described for A, B, C but for the beta band.

Figure 7. Spectral analysis of BVPs during constant velocity VS. A, Scalp map of early alpha band power compared to late in response to counterclockwise rotation only showed weak alpha band suppression without clear topography. B, Scalp map of p-values showed no significant electrodes when comparing early and late alpha band power as done for healthy subjects. Topography of electrodes with strongest response were not clustered. C, Early alpha band power normalized to late period for counterclockwise rotation (black bar) and static baseline (grey bar) for the average of all electrodes. D, E, F Same analysis as described for A, B, C but for the beta band. There were no significant modulations in the alpha or beta bands for the BVPs.

Figure 8. Comparison of spectral modulations between healthy subjects and BVPs in response to constant velocity rotation. A, Early vs. late alpha power during counterclockwise rotation is significantly lower in healthy subjects (blue bar) than in BVPs (red bar). B, The same analysis as in A, but for the beta band. Beta band power in healthy subjects was not statistically different from BVPs.
Figure 9. Neural generators of vestibular alpha suppression during constant velocity VS. Linear inverse solution of early versus late alpha band power during counterclockwise rotation in healthy subjects. Voxels are shown in blue for suppression, and red for enhancement.

Figure 10. Evoked potentials by transient VS. A, Grand average of evoked potentials for healthy subjects (blue trace) and BVPs (red trace) using the same preprocessing regime as previous studies (see results for references). Note that the evoked potentials recorded for healthy subjects and BVPs do not differ. Grey line is the acceleration profile. B, Grand average of evoked potentials after recordings were re-referenced to an average reference and artefact removal using FASTER. Black trace is the difference between healthy subjects and BVPs.