The human vestibular cortex

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Introduction: The cortical representations for almost all senses (touch, pain, sound, vision and smell) have been robustly mapped in humans with functional neuroimaging. But the majority of cerebral regions receiving or processing vestibular information originating from our so-called sixth sense have evaded a definitive localization for more than two decades now. Neuron recordings and tracer studies in several primate species had previously established a cortical vestibular network of at least seven (potentially ten) regions per hemisphere (Fig.1)[1, 2]. Up to now, several methodological obstacles seem to have impeded a dedicated delineation of the homologues of a human vestibular cortex. These included somatosensory and autonomic confounders especially in the operculo-insular region, slice- and not volume-specific head motion artifacts (interaction of vestibular stimulus profile and TR), difficulties in evoking an actual naturalistic vestibular percept, low statistical power and general spatio-temporal limitations of fMRI. Aim of our fMRI study was to finally localize all cortical vestibular regions known from other primate species in humans. In a subsequent step we also intended to perform an internal replication and verification of our findings in an independent cohort.

Methods: We examined 138 right-handed healthy subjects (68F; mean age 27 years) in two separate groups (main group n=75 (outlier exclusion n=3, internal replication group n=60) spanning a cultural background of 17 different nationalities. Sinusoidal (0.875Hz) and ramp-like low-frequency galvanic vestibular stimulation (GVS) (3mA) after local anaesthesia of the postauricular region was conducted via bimastral electrodes to elicit naturalistic vestibular sensations. Structural and functional images were obtained in a clinical 3T scanner (Siemens Magnetom Skyra) equipped with a 64-channel head and neck coil. The protocol included a resting-state and a GVS session consisting of a prescan-normalized T2*-weighted EPI sequence (TR 700ms, 56 interleaved slices, MB 6, 2.5mm in-plane resolution, slice thickness 2.5 mm), as well as a structural MPRAGE sequence. Data analysis was performed using SPM12 (Version 7219 Wellcome Department of Imaging Neuroscience, UK) and the SPM Anatomy toolbox (Version 2.2c) after standard preprocessing including DARTEL-based normalization [3]. Results were considered significant at FDR p<0.01 (corrected at voxel level).

Results: Controlling and accounting for somatosensory, nociceptive and salience effects in the inferior frontal gyrus, the anterior and middle insula and area OP1/3 (Fig.3) we were able to delineate and identify ten cortical homologues to known vestibular representations in non-human primates (Fig. 2). Aside from the vestibular nuclei and cerebellar nodule and uvula we found cytoarchitectonic area OP2 in the parietal operculum to be the human core equivalent to the parieto-insular vestibular region PIVC. Monkey visual posterior sylvian area (VPS) could be mapped to cytoarchitectonic area PFcm whereas area 7 is probably located in the human inferior parietal lobule (cytoarchitectonic area PF). We could also identify the ventral intraparietal area (VIP) in the intraparietal sulcus (cytoarchitectonic area HIP3) as well as areas 2v and 3aV. The area cingulate sulcus visual (CSv) was found to be the homologue to the vestibular cingulate (VC) region known from non-human primates. We also found a strong vestibular response in the visualmotion-oculomotor area MST and could map the vestibular monkey area 6 to a lateral premotor region in humans. The vestibular response found in the periarculate cortex in monkeys is probably reflected in an anterior-paramedian human activation within the supplementary motor area in direct proximity to the supplementary eye field. We found no dedicated unimodal vestibular region in the insular cortex.

Fig. 1: Schematic drawing of the known cortical vestibular areas in a rhesus monkey brain: (top) periarculate cortex, areas 6, 3aV (3aHV: 3a-hand-vestibular region, 3aNv: 3a-neck-vestibular region), 2v, VIP: ventral intraparietal area, MIP: medial intraparietal area, area 7, VPS: visual posterior sylvian area, MST: medial superior temporal area, PIVC: parieto-insular vestibular cortex; (bottom) VC: vestibular cingulate area. Synthesis and adaption from [1, 4, 5].

Fig.2: The entire central vestibular system after naturalistic stimulation in a large cohort (n=75). All scales represent z-scores.

Fig.3: Conjunction analysis of a mastoidal sham stimulation and GVS shows significant activations in somatosensory area OP1, adjacent area PFcm, OP3, the rolandic operculum (RO) and the anterior and middle insula as part of the salience network (IN).

Conclusion: We were able to robustly delineate and map the entire human vestibular cortex. We identified ten cortical homologue vestibular regions known from non-human primates. The general response patterns to our confounder-minimised GVS protocol show that the core cortical vestibular network in humans is probably represented by areas OP2 (PIVC), MST, PFcm (VPS), PF (area 7) and CSv (VC).

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