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Neural correlates of hemispheric dominance and ipsilaterality within the vestibular system

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ABSTRACT

Earlier functional imaging studies on the processing of vestibular information mainly focused on cortical activations due to stimulation of the horizontal semicircular canals in right-handers. Two factors were found to determine its processing in the temporo-parietal cortex: a dominance of the non-dominant hemisphere and an ipsilaterality of the neural pathways. In an investigation of the role of these factors in the vestibular otoliths, we used vestibular evoked myogenic potentials (VEMPs) in a fMRI study of monaural saccular-otolith stimulation. Our aim was to (1) analyze the hemispheric dominance for saccular-otolith information in healthy left-handers, (2) determine if there is a predominance of the ipsilateral saccular-otolith projection, and (3) evaluate the impact of both factors on the temporo-parieto-insular activation pattern. A block design with three stimulation and rest conditions was applied: (1) 102 dB-VEMP stimulation; (2) 65 dB-control-acoustic stimulation, (3) 102 dB-white-noise-control stimulation. After subtraction of acoustic side effects, bilateral activations were found in the posterior insula, the superior/middle/transverse temporal gyri, and the inferior parietal lobule. The distribution of the saccular-otolith activations was influenced by the two factors but with topographic disparity: whereas the inferior parts of the temporo-parietal cortex were mainly influenced by the ipsilaterality of the pathways, the upper parts reflected the dominance of the non-dominant hemisphere. This is in contrast to the processing of acoustic stimulation, which showed a predominance of the contralateral pathways. Our study proves the importance of the hemispheric preponderance also in left-handers, which is of relevance in the superior parts of the insula gyrus V, the inferior parietal lobule, and the superior temporal gyri.

Introduction

Strong evidence from animal studies indicates that a network of several distinct areas in the temporo-parietal cortex participate in the processing of vestibular information, for example, area 2v (Fredrickson et al., 1966; Büttner and Buettner, 1978), area 3aV (Phillips et al., 1971; Schwarz et al., 1973; Ödkvist et al., 1974), the multisensory parieto-insular vestibular cortex (PIVC) in the posterior insula/retroinsular region (Grüsser et al., 1990), the cingulum, the periarcuate area 6pa (Ebata et al., 2004), parts of area 7 (Faugier-Grimaud and Ventre, 1989), the visual posterior sylvian area (VPS) (Guldin and Grüsser, 1998), and the ventral intraparietal area (VIP) (Bremmer et al., 2002; Schlack et al., 2005). During the last 10 years several functional imaging (PET and fMRI) studies in humans using caloric irrigation of the horizontal semicircular canals or sinusoidal, bimastoidal galvanic stimulation of the vestibular nerve have also revealed a cortical network that processes vestibular information in the temporo-parietal cortex bilaterally, which is similar to the one found in monkeys (Bucher et al., 1998; Lobel et al., 1998; Bense et al., 2001; Suzuki et al., 2001; Bremmer et al., 2001; Fasold et al., 2002; Dieterich et al., 2003; Stephan et al., 2005). The insula and its adjacent cortices are of special interest, since activations during vestibular stimulation were widely distributed from the inferior insula (Dieterich et al., 2005), via the posterior and the retroinsular region as well as the adjacent inferior parietal lobule up to the superior temporal and parietal cortices (Suzuki et al., 2001; Bense et al., 2001; Stephan et al., 2005). All these areas were activated in both hemispheres, but there was a predominance in the temporo-parietal areas of the right hemisphere in right-handed healthy subjects during stimulation of the horizontal semicircular canal (Fasold et al., 2002; Dieterich et al., 2003). Besides this dominance of the non-dominant hemisphere, a PET study using caloric irrigation showed that a second factor determines the processing of vestibular information at cortical level: a predominance of the pathways to the hemisphere ipsilateral to the irrigated ear (Dieterich et al., 2003). These studies were performed primarily with right-handers and used caloric irrigation, which mainly activates the horizontal semicircular canal fibers. Only recently, Miyamoto and co-workers (2005, 2007) studied the saccular-otolith projections to fronto-temporo-parietal regions of the human cortex in

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a first attempt via vestibular evoked myogenic potentials (VEMPs). Indeed, in a systematic analysis of the whole brain, VEMPs were proven to activate a similar bilateral network in the temporo-parietal cortex in fMRI, which also showed a dominance of the right hemisphere in right-handers (Schlindwein et al., 2008), as was found during vestibular semicircular canal stimulation. Thus, the question arose as to whether saccular-otolith information is processed subject to a predominance of both the non-dominant hemisphere and the ipsilateral pathways. This is of special importance, since the click-evoked potentials of saccular-otolith (VEMPs) are elicited by monaural acoustic signals, which are processed mainly by the contralateral hemisphere. Thus, the click-evoked saccular potentials are per se a combination of acoustic stimulation and vestibular saccular-otolith stimulation. This requires subtraction of the acoustic control condition to isolate the saccular-otolith component and its processing pathways.

The aims of the present study using saccular-otolith stimulation in healthy left-handed subjects were threefold:

1. to analyze the hemispheric dominance in left-handers for saccular-otolith information,
2. to verify the predominance of the ipsilateral vestibular saccular-otolith projections to the temporo-parietal areas, and
3. to evaluate the impact of both factors on the different parts of the widespread activations in the temporo-parietal cortex of both hemispheres (i.e., which areas are more influenced by the ipsilaterality of the pathways, and which by the hemispheric dominance).

Methods and materials

Subjects

Sixteen healthy left-handed volunteers (9 women, 7 men; mean age 25.6 years, range 22 to 33 years) without any history or complaints of neurological or neuro-otological dysfunction participated in the study. None of the subjects reported concurrent use of any medication. Methods were identical to those applied earlier in right-handers (Schlindwein et al., 2008). Individual sound level thresholds and thresholds for VEMPs were determined before the experiment, while subjects lay in an identical supine position outside the scanner. All subjects showed reproducible VEMPs at 85 dB but none at 65 dB sound pressure level (SPL) while lying in a supine position without head elevation or rotation. The VEMPs were recorded from surface electrodes over the sternocleidomastoid muscles (Colebatch et al., 1994). Registration of VEMPs outside the scanner only served as a control for the application of the saccular-otolith stimulation, since they reflect the activation of the vestibulospinal projections. Only subjects with normal hearing thresholds and physiological shapes and amplitudes of VEMPs without relevant side difference (<30% amplitude) were included. The Laterality Quotient of handedness according to the 10-item inventory of the Edinburgh test (Oldfield, 1971; Salmaso and Longoni, 1985) was −100 in 11 and −80 in five subjects; thus all subjects were strongly left-handed. This study was carried out in accordance with the Helsinki Declaration and approved by the local ethics committee. All subjects gave their informed written consent.

Vestibular stimulation by vestibular evoked myogenic potentials

Vestibular evoked myogenic potentials elicited by air-conducted short tone bursts (STB) – also called click-evoked potentials – represent the saccular-otolith mediated, short-latency vestibulocollic reflex, which stabilizes the head on the trunk in space. During the STB the saccular-otolith of one labyrinth reacts to loud click sounds of 85–130 dB SPL, and the signal is forwarded via the inferior portion of the vestibular nerve to the vestibular nuclei in the brainstem and further to α-motoneurons of the vestibulospinal tract (Brantberg and Mathiesen, 2004; Basta et al. 2005). Habituation has not been reported to affect the recorded potentials (Wu and Murofushi, 1999).

The differential effects of unilateral, right- and left-sided VEMP stimulation were examined by fMRI while the contralateral ear was plugged. The tone burst signal was similar to that used in a clinical setting: it had a frequency of 500 Hz, a rise and fall time of 1 ms, and a plateau time of 8 ms in order to guarantee optimal saccule stimulation (Cheng and Murofushi, 2001a,b; Akin et al., 2003). The stimulus was presented at a repetition rate of 3 Hz. The tone burst signal was created with the help of a digital audio editor (Goldwave Software Version 5.08, St. John's, Canada). All subjects lay in a supine position without head elevation or rotation, since a preceding study with right-handers had proven that the continuous tonic activation of the sternocleidomastoid muscle throughout the whole experiment did not influence the pattern of cortical activation during VEMP (Schlindwein et al., 2008). This muscle activation is only needed to enhance the response amplitude of the VEMP (Akin et al., 2004).

Each volunteer underwent one continuous session with three different stimulation conditions and rest condition (without any stimulation) that were applied in a block design to each ear: (1) a 102 dB SPL A 500 Hz tone burst signal, which induced VEMPs; (2) a control with an identical tone burst signal below threshold 65 dB, which did not trigger VEMPs; and (3) a white noise signal at 102 dB as a control for the loudness of VEMP stimulation with the same sound pressure level. The order and sides of the unilateral stimulations were randomized for each subject.

MRI acquisition

The subjects were positioned in the circularly polarized head coil in a clinical 1.5 T scanner (Siemens Magnetom Vision, Erlangen, Germany) wearing MRI-suitable piezo-electric headphones (Jaencke, Zuerich). The sealed headphones measurably suppressed scanner noise for the subject to well below 45 dB SPL, thus overcoming the intrinsic acoustic fMRI problem of gradient noise. To reduce head movements and consequently artificial activation patterns during data acquisition (Friston et al., 1996), the subject's forehead was taped to the coil. Subjects were asked to passively experience the stimuli and to lie in a relaxed position with their eyes closed for the whole experiment in an otherwise completely darkened scanner room. Each scanning session comprised three successive trials consisting of 172 volumes, each in 13 alternating blocks of seven images at rest without any stimulation and six images during the different sound stimulations. Each volume consisted of 40 slices of a T2*-weighted interleaved echo-planar imaging (EPI) sequence (TR = 4.2 s, TE = 60 ms, FOV = 192–220 mm, image matrix = 64^2, slice thickness = 4 mm), covering the whole brain. A sparse sampling technique was not used, because the good suppression of the scanner noise by our modified head phones and the inevitably high repetition rate of our stimulus produced statistically better results in a continuous setup. All images were collected parallel to the AC–PC line. The first three volumes of each trial were discarded to eliminate spin saturation effects.

Data analysis

fMRI data were processed using Pentium IV workstations running on Windows 2000 or XP®. The fMRI data sets were reconstructed offline, and then converted into the file format that was analyzed using Statistical Parametric Mapping software (SPM2, Wellcome Department of Imaging Neuroscience, London 2005). The images were realigned to the first one of each scanning session to correct for subject movement and were then stereotactically normalized into the standard anatomical space defined by the Montreal Neurological Institute (MNI) template by means of linear and non-linear transformation (Friston et al., 1995a). Thus, all stereotactic coordinates given in this paper refer to the MNI coordinate system. During