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Research paper

Neural correlates of human somatosensory integration in tinnitus

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ABSTRACT

Possible neural correlates of somatosensory modulation of tinnitus were assessed. Functional magnetic resonance imaging (fMRI) was used to investigate differences in neural activity between subjects that can modulate their tinnitus by jaw protrusion and normal hearing controls. We measured responses to bilateral sound and responses to jaw protrusion. Additionally we studied multimodal integration of somatosensory jaw protrusion and sound. The auditory system responded to both sound and jaw protrusion. Jaw responses were enhanced in the cochlear nucleus (CN) and the inferior colliculus (IC) in tinnitus patients. The responses of the auditory brain areas to jaw protrusion presumable account for the modulation of tinnitus as described by the patients. The somatosensory system responded to jaw protrusion and not to sound. These responses occurred both in subjects with tinnitus and controls. Unexpectedly, the cerebellum responded to sound in normal hearing subjects, but not in tinnitus patients. Together, these results provide a neurophysiological basis for the effect of jaw protrusion on tinnitus.

1. Introduction

Tinnitus is an auditory sensation without the presence of an external acoustic stimulus. Almost all adults have experienced some form of tinnitus, mostly transient in nature. The exact etiology of tinnitus remains unknown but may involve increased spontaneous neural activity, increased neural synchrony or reorganized tonotopic maps as a neural substrate of tinnitus in humans (Eggermont, 2006).

Tinnitus is affected in complex ways by somatosensory influences. Somatic maneuvers can elicit tinnitus or modulate the psychoacoustic attributes of tinnitus (e.g., the loudness or pitch). Examples of these somatosensory modulators are forceful head and neck contractions (Levine, 1999; Levine et al., 2003, 2008; Abel and Levine, 2004), oral facial movements like jaw clenching or jaw protrusion (Chole and Parker, 1992; Rubinstein, 1993; Lockwood et al., 1998; Pinchoff et al., 1998), electrical stimulation of the median nerve (Møller et al., 1992; Møller and Rollins, 2002) and cutaneous stimulation (Cacace et al., 1999a,b). In a remarkable case, finger movement evoked tinnitus (Cullington, 2001). A change of gaze is also known to modulate tinnitus in some patients with a vestibular schwannoma removed (Cacace et al., 1994a,b; Giraud et al., 1999; Coad et al., 2001; Lockwood et al., 2001; Herraiz et al., 2003; Albuquerque and Bronstein, 2004; Baguley et al., 2006), which is possibly caused by somatosensory neural signals.

Somatic modulation or induction of tinnitus may be considered a special case of multisensory integration – a phenomenon, in which one (sensory) modality influences another. Examples of this multisensory integration are visual stimuli that modulate activity measured in the auditory cortex (Pekkola et al., 2005) and audio-visual speech or communication signals that modulate activity in the auditory cortex (Calvert et al., 1999; Ruytjens et al., 2006, 2007). In addition to auditory-visual integration, there are studies that specifically assess multisensory integration between the auditory system and the somatosensory system. One illustrative example is a study of Jousmaki and Hari (1998) showing that auditory input can modulate touch sensation. Subjects were asked to rub their hands, and the evoked sounds were played back to them. When the high-frequency content of this auditory signal was increased in loudness, subjects felt the skin under their palms becoming dry – the parchment-skin illusion.

Abbreviations: AAC, auditory association cortex; BA, Brodmann area; BOLD, blood oxygen level dependent; CN, cochlear nucleus/nuclei; EPI, echo planar imaging; fMRI, functional magnetic resonance imaging; HL, hearing level; IC, inferior colliculus/colliculi; MGB, medial geniculate body of the thalamus; PAC, primary auditory cortex; Put, putamen; ROI, region of interest; SII, secondary somatosensory cortex; SPM, statistical parametric map; TE, echo time; TR, repetition time; VL, ventrolateral.

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Somatosensory stimulation can also influence auditory perception. The fact that subjects with somatosensory tinnitus can modulate their tinnitus is an example of this somatosensory-auditory modulation, and might be explained by changes in normal multisensory integration. Noise-induced hearing-loss, for example, has been reported to alter the normal somatosensory input. The somatosensory input to the cochlear nucleus (CN) is increased after hearing loss (Shore et al., 2008). This change in balance in somatosensory and auditory input at the level of the brainstem might thus be the neural correlate of somatosensory modulation of tinnitus.

Functional magnetic resonance imaging (fMRI) methods have been used to study multisensory integration of auditory and somatosensory input in the auditory cortex of the macaque monkey. Kayser et al. (2005) showed multisensory integration of tactile stimuli of the palm and the foot, and auditory stimuli in the belt area (caudal medial and caudal lateral belt area) of the auditory cortex. Supra-additive effects were demonstrated in the belt area, showing voxels with a response to the multisensory stimuli that was larger than the sum of the unisensory stimuli. Foxe et al. (2002) used an fMRI design to assess multisensory integration in humans. The unisensory response to sound and somatosensory stimulation was determined. There were voxels that showed overlap in activity between the two conditions. A cluster showing overlap was determined as the posterior part of the left superior temporal gyrus (Brodmann area (BA) 22 and 39) and the right auditory association cortex (BA22). Within the left-hemisphere a small area was found where the bimodal response exceeded the summed unimodal responses (e.g., a supra-additive effect). Schurmann et al. (2006) later used vibrotactile, pulsed tactile and white noise auditory stimuli in an fMRI design to assess human multisensory integration. In the posterior auditory belt area, bilateral areas were found that showed overlap in activity between the unisensory conditions. These were the same area as found by Foxe et al. (2002), showing voxels with overlap between tactile and auditory stimuli.

Multisensory integration and spatial overlap of auditory and somatosensory input was also shown in several parts of the auditory system using anatomical labeling methods and electrophysiological measurements. Sites of neurophysiologic auditory-somatosensory integration were identified in the lower brainstem (the dorsal and ventral CN) and the inferior colliculus (IC) in guinea pigs (see review by Dehmel et al. (2008)). In addition, multisensory areas (i.e., areas that receive both auditory and somatosensory input, but not necessarily exhibit multisensory integration) were found in macaque monkeys using anatomical labeling methods. These areas were identified as the medial geniculate complex and the caudal medial belt area of the auditory cortex (Schroeder et al., 2001; Smiley et al., 2007; Hackett et al., 2007a,b). These studies suggest that somatosensory-auditory integration may already take place at the brainstem auditory nuclei.

In this work we investigated the phenomenon of somatic modulation of tinnitus. For this purpose, we studied two groups of subjects: normal controls and subjects with tinnitus. The subjects in the tinnitus group were included based on their ability to change the psychoacoustical characteristics of their tinnitus by jaw protrusion. We hypothesize that this may be based on somatosensory-auditory interaction already in the brainstem.

2. Materials and methods

2.1. Subjects

Thirteen subjects (12 males and one female, age 28–68 years, median 52 years) with tinnitus were recruited at the University Medical Center Groningen in the multidisciplinary tinnitus outpatient clinic, all with no known neurological and psychiatric history. The subjects with tinnitus were selected based on their ability to alter the loudness or pitch of their tinnitus by performing a protrusion of the jaw. Additionally, twenty control subjects (18 males and two females, age 20–59 years, median 31 years) without tinnitus were recruited. A selection criterion for all subject comprised the hearing levels for both ears better than 30 dB hearing levels (HL) for frequencies 250, 500 and 1000 Hz, with the average difference between the left and right ear not exceeding 10 dB.

In the patient group, the perceived tinnitus frequency and loudness level were determined by a matching procedure. The frequency matching was performed with an external tone presented at the non-tinnitus ear or at the ear where the tinnitus was weakest, at a comfortable level. The loudness level was then determined by adjusting the level of this tone to match the tinnitus loudness.

Somatosensory modulation of tinnitus was assessed using a questionnaire as described in Table 2. In this questionnaire—presented here as a translated version of the original Dutch version, the loudness of the tinnitus and loudness of the tinnitus during jaw protrusion was assessed using a visual analog scale. In addition to these loudness values, subjects were asked to rate the duration (in seconds) of the period that subject could pertain the jaw protrusion that lead to a change of their tinnitus. Subjects reported loudness values prior to the fMRI study (see Fig. 4). Subjects without tinnitus were also asked to report any perceptual change corresponding to jaw protrusion but no changes were reported.

The handedness of each subject was determined using a translated version of the Edinburgh inventory (Oldfield, 1971). Details of most subject characteristics are shown in Table 1 and the assessment of the somatosensory modulation can be found in section 2. The study was approved by the local medical ethics committee and written informed consent was obtained for each participant.

2.2. MRI protocol

All imaging experiments were performed on a 3T MRI system (Philips Intera, Philips Medical Systems, Best, The Netherlands)

Table 1
Subject characteristics.

Characteristics	Controls ($n = 20$)	Subjects with tinnitus ($n = 13$)
Age (years)		
Average	32.8	51.8
Standard deviation	10.5	10.4
range	20–59	28–68
Gender		
Male	18 (90%)	12 (82%)
Tinnitus		
Lateralization (left/right/non-lateralized)	–	1/1/11
Average pitch (Hz)	–	6400
Range (Hz)	–	750–12,000
Average loudness (dB SL)	–	16.7
Range (dB SL)	–	10–25
Modulation of tinnitus		
Changes in frequency	–	2 (15%)
Changes in loudness	–	10 (77%)
Changes in frequency and loudness	–	1 (8%)
Handedness		
Right handed	19 (95%)	11 (85%)
Left handed	1 (5%)	1 (8%)
Ambidextrous	–	1 (8%)