

Processing of Spatial and Nonspatial Auditory Information in the Human Brain

Irina Anurova

Academic dissertation

*To be publicly discussed with permission of the Medical Faculty
of the University of Helsinki
at the Lecture Hall 2 of Biomedicum Helsinki,
Haartmaninkatu 8,
on June 15th, 2005, at 12 noon.*

Neuroscience Unit, Institute of Biomedicine/Physiology, University of Helsinki, Finland

BioMag Laboratory, Helsinki University Central Hospital, University of Helsinki, Finland

Helsinki 2005

Supervised by

Docent Synnöve Carlson,
Neuroscience Unit,
Institute of Biomedicine/Physiology,
University of Helsinki, Finland

Reviewed by

Professor Heikki Hämäläinen,
Center for Cognitive Neuroscience,
Department of Psychology,
University of Turku,
Finland

and

Docent Jari Karhu,
Department of Clinical Neurophysiology,
Kuopio University Hospital,
Kuopio, Finland

Official Opponent

Docent Jyrki Mäkelä,
BioMag Laboratory,
Helsinki University Central Hospital,
University of Helsinki, Finland

ISBN 952-91-8743-2 (nid.)
ISBN 952-10-2480-1 (PDF)

Yliopistopaino
Helsinki 2005

TABLE OF CONTENTS

LIST OF ORIGINAL PUBLICATIONS	5
ABBREVIATIONS	6
SUMMARY	7
1. INTRODUCTION	8
2. REVIEW OF LITERATURE	10
2.1. Auditory pathways	10
2.2. Processing of spatial and nonspatial auditory information	15
2.2.1. Processing of spectro-temporal characteristics	15
2.2.1.1. Frequency.....	15
2.2.1.2. Intensity.....	16
2.2.1.3. Duration	16
2.2.1.4. Stimulus complexity	17
2.2.1.5. Temporal regularity.....	18
2.2.2. Processing of auditory spatial information.....	19
2.2.2.1. Localization of stationary sounds	19
2.2.2.2. Processing of sound motion.....	22
2.3. Auditory long-latency evoked responses	24
2.3.1. N1	24
2.3.2. P2.....	29
2.3.3. N2.....	29
2.3.4. P3 and Positive Slow Wave (PSW).....	31
3. AIMS OF THE STUDY	35
4. MATERIALS AND METHODS	36
4.1. Subjects	36
4.2. Stimuli	36
4.3. Tasks	37
4.4. Data collection and analysis	40
4.5. Summary of methods	45
5. RESULTS	46
Study I. Effect of selective interference on auditory working memory processing	46
Study II. Effect of memory load and auditory stimulus attribute on the cortical distribution of late slow waves	47
Behavioral data	47
Late slow waves.....	48
Study III. Effect of the auditory stimulus attribute on electric and magnetic counterparts of the auditory N1	48
Behavioral data.....	48
EEG data.....	49
MEG data.....	51

Studies IV-V. Effect of memory load on electric and magnetic counterparts of auditory evoked responses recorded during spatial and nonspatial task performance.....	53
Behavioral data.....	53
Responses to memory cues (study IV).....	53
EEG data.....	53
MEG data.....	56
Responses to probes (study V).....	57
EEG data.....	57
MEG data.....	58
6. DISCUSSION.....	61
6.1. Evidence for dissociation between spatial and nonspatial auditory information processing obtained at the behavioral level.....	61
6.2. Effect of memory load but not type of task on the Late Slow Waves.....	62
6.3. Effect of task on transient auditory evoked responses: evidence for dissociation between spatial and nonspatial auditory information processing obtained at the electrophysiological level.....	63
6.3.1. The N1 component in matching-to-sample task.....	63
6.3.2. The N1 component in 3-back/DMTS task.....	65
6.3.3. Effect of memory load on task-related differences.....	66
6.3.4. Effect of task on cortical generators of slow endogenous components, the P3 and PSW, elicited in the responses to probes.....	67
7. CONCLUSIONS.....	70
ACKNOWLEDGEMENTS.....	71
REFERENCES.....	72

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on five publications, which are referred to in the text by the Roman numerals I – V.

- I. Anourova I., Rämä P., Alho K., Koivusalo S., Kalmari J., Carlson S. 1999. Selective interference reveals dissociation between auditory memory for location and pitch. *NeuroReport* 10: 3543-3547.
- II. Rämä P., Paavilainen L., Anourova I., Alho K., Reinikainen K., Sipilä S., Carlson S. 2000. Modulation of slow brain potentials by working memory load in spatial and nonspatial auditory tasks. *Neuropsychologia* 38: 913-922.
- III. Anourova I., Nikouline V. V., Ilmoniemi R. J., Hotta J., Aronen H. J., Carlson S. 2001. Evidence for dissociation of spatial and nonspatial auditory information processing. *NeuroImage* 14: 1268-1277.
- IV. Anurova I., Artchakov D., Korvenoja A., Ilmoniemi R.J., Aronen H.J., Carlson S. 2003. Differences between auditory evoked responses recorded during spatial and nonspatial working memory tasks. *NeuroImage* 20: 1181-1192.
- V. Anurova I., Artchakov D., Korvenoja A., Ilmoniemi R.J., Aronen H.J., Carlson S. Cortical generators of slow evoked responses elicited by spatial and nonspatial auditory working memory tasks. *Clinical Neurophysiology*. In press.

ABBREVIATIONS

AI – auditory area I
AM – amplitude modulation
ANOVA – analysis of variance
CN – cochlear nuclei
CM, CL, ML, AL, RTL, RTM and RM – caudomedial, caudolateral, middle lateral, anterolateral, lateral rostrotemporal, medial rostrotemporal and rostromedial belt areas
DM, DL and PL – dorso-medial, dorso-lateral and postero-lateral thalamic nuclei
DMTS – delayed matching-to-sample
ECD – equivalent current dipole
EEG – electroencephalogram
EOG – electrooculogram
ERP – event-related potential
FM – frequency modulation
fMRI – functional magnetic resonance imaging
HG – Heschl's gyrus
IC – inferior colliculi
IFG – inferior frontal gyrus
IID/ITD – interaural intensity/time difference
IPL – inferior parietal lobe
ISI – interstimulus interval
L, M, R – left, middle, right
LSW – late slow wave
MEG – magnetoencephalogram
MGB – medial geniculate bodies
MGv, MGd and MGm – ventral, dorsal and medial nuclei of the medial geniculate complex
MRI – magnetic resonance image (imaging)
MTG – medial temporal gyrus
PET – positron emission tomography
PSW – positive slow wave
PT – planum temporale
R and RT – rostral and rostro-temporal auditory areas
RTs – reaction times
SEM – standard errors of mean
SFS – superior frontal sulcus
SOC – superior olivary complex
SPL – sound pressure level
STG/STS – superior temporal gyrus/sulcus
Tpt – temporo-parietal area

SUMMARY

The neuronal mechanisms underlying the processing of sound content and its spatial location have attracted research interest over the last decade. In recent years, a dual-stream model, which assumes segregation of “what” and “where” auditory information processing, has gained some support. Anatomical tracing and electrophysiological single-cell studies in nonhuman primates provide basis for the segregation. Reports on patients with selective deficits in sound localization and recognition following focal hemispheric lesions and results from neuroimaging and behavioral studies suggest that different brain structures are specifically involved in the processing of spatial and nonspatial information.

The present project aimed to test the hypothesis of segregation of “what” and “where” auditory information processing both at behavioral level and by using electrophysiological evoked response recordings during the performance of auditory spatial and nonspatial working memory tasks. Another question addressed in the present project concerned the effect of memory load on the segregation between spatial and nonspatial information processing. Two electrophysiological research techniques, electroencephalography (EEG) and magnetoencephalography (MEG), were used to investigate the timing and location of the possible segregation. The use of these techniques, characterized by excellent time resolution and relatively good localization ability, enabled to address not only the issue of dissociation between “what” and “where” information processing in the auditory system but also the question “where” and “when” the possible dissociation takes place in the human brain.

The results of the five studies included in the present project suggest that there is segregation between spatial and nonspatial information processing in the auditory neuronal networks. This segregation depends on mnemonic demands; the task-related (spatial vs. nonspatial) differences were observed at moderate but not high memory load levels. The differences between the evoked responses recorded during the location and pitch tasks were seen at the time range of long-latency evoked responses up to and including the positive slow wave (PSW), but not during Late Slow Waves. This finding suggests that partially separate neuronal networks are involved in the attribute-specific analysis of auditory stimuli and their encoding into working memory, whereas the maintenance of auditory information is accomplished by a common, nonspecific neuronal network. Finally, results of the source modeling of the MEG data suggest that dissociation between spatial and nonspatial information processing takes place in the auditory cortex on the supratemporal plane during the generation of the N1 component and in associative temporal areas in the posterior and middle parts of the superior temporal sulcus during the generation of slow evoked responses (the P3 and PSW).

1. INTRODUCTION

The auditory system provides us a remarkable ability to distinguish a great variety of sounds and localize their sources. The auditory functions form the basis of communication and spatial orientation and are essential for the adaptation to the social and physical environment.

Several lines of evidence suggest that visual information processing is segregated into the ventral “What” and dorsal “Where” neuronal pathways. This dual-stream model was proposed over two decades ago and has been supported by studies in humans and animals (Mishkin et al., 1983, Courtney et al., 1996, Smith et al., 1995, Vuontela et al., 1999, Wilson et al., 1993). However the question whether the processing of sounds is also parcelled into spatial and nonspatial domains remains open (Kaas and Hackett, 1999, Cohen and Wessinger, 1999, Belin and Zatorre, 2000, Romanski et al., 2000, Rauschecker and Tian, 2000, Middlebrooks, 2002).

At the time when this project was initiated there was not much knowledge about the possible segregation of spatial and nonspatial auditory information processing. Electrophysiological and anatomical findings provided a basis for the dual-stream theory. Parallel input from distinct thalamic nuclei to different primary and nonprimary auditory areas was demonstrated in a combined electrophysiological and anatomical tracing study in nonhuman primates (Rauschecker et al., 1997). Parallel neuronal pathways originating in separate nonprimary auditory fields and terminating in distinct regions of the frontal lobes (Kaas and Hackett, 1998, Kaas et al., 1999, Romanski et al., 1999) had also been documented. Furthermore, connections between the lateral belt of the auditory cortex and the prefrontal cortex via parietal areas were demonstrated in the study by Romanski et al. (1999), suggesting a “potentially spatial” dorsal auditory pathway analogous to the dorsal visual route.

A behavioral study by Clarke et al. (1998) was one of the first investigations in which spatial and nonspatial auditory working memory tasks were directly contrasted. The authors showed that auditory working memory for sound content was more disrupted by a sound recognition than a sound localization interference task, whereas auditory memory for sound location was nonselectively disrupted by both spatial and nonspatial interference. These results provided some evidence for partial segregation of spatial and nonspatial auditory information processing.

In recent years, the hypothesis of dissociation of auditory information processing into distinct neuronal pathways has gained some further support. Reports on clinical cases have demonstrated that focal right hemispheric lesions might cause selective deficits in sound localization and recognition (Clarke et al., 2002). Patients with normal sound localization but impaired recognition had lesions involving the inferior parietal and frontal cortices, whereas when the lesion affected the anterior part of the temporal lobe, patients had spared localization abilities but difficulties in recognizing sounds.

Neuroimaging has also provided support for the idea of segregation. Several recent studies have shown participation of parietal areas in both visual and auditory localization

(Carlson et al., 1998, Martinkauppi et al., 2000, Bushara et al., 1999). Results from an fMRI study by Maeder et al. (2001) suggest that different brain structures are specifically activated during the processing of the content and spatial location of sound. However, due to the varying demands of the tasks contrasted in their study and the characteristics of the stimuli used, it is possible that the finding does not unequivocally imply differences in the processing of sound content and its location. In a recent combined fMRI and electrophysiological study by Alain et al. (2001), spatial and nonspatial tasks were carefully balanced, had identical stimuli, and differed from each other only with respect to the instructions defining the relevant stimulus attribute. Despite the differences in the methodological design and the physical features of stimuli used in the studies by Maeder et al. (2001) and Alain et al. (2001), the main findings were, however, rather similar: nonspatial auditory information processing produced stronger activation in the nonprimary auditory cortex and inferior frontal gyrus, while spatial auditory processing preferentially activated the inferior parietal cortex. Taken together, these two studies support the idea of dissociation of auditory information processing into two specialized streams, similar to the ventral and dorsal pathways in the visual system.

On the other hand, in a positron emission tomography (PET) study on auditory selective attention by Zatorre and colleagues (1999), in which subjects were required to attend either to the location or frequency of a sound, a common nonspecific right-hemispheric network was shown to be involved in both spatial and nonspatial processing. These results suggest that auditory information processing is integrated rather than parcelled into spatial and nonspatial domains. However, it is also possible that the same cortical areas mediate both audiospatial and sound content information but distinct areas are preferentially activated during one or the other type of information processing (Cohen and Wessinger, 1999, Weeks et al., 1999). A recent functional magnetic resonance imaging (fMRI) study by Zatorre's group (2002) revealed that varying the spatial distribution of the simultaneously presented sounds significantly modulated activation in the posterior part of the superior temporal gyrus when the sounds possessed object-related features. The authors concluded that spatial sensitivity might be linked to the spectrotemporal features of the stimulus, and "rather than being strictly segregated, object-related and spatial information may interact within the dorsal pathway" (Zatorre et al., 2002).

The present research project aimed to test the hypothesis that the processing of auditory information is dissociated into spatial and nonspatial domains. Electroencephalography (EEG) and magnetoencephalography (MEG) were used, because these techniques enable accurate assessment of the timing of task-related differences and also localization of the cortical areas preferentially involved in one or another type of information processing.

2. REVIEW OF LITERATURE

2.1. Auditory pathways

When a sound reaches our ears, its mechanical energy is captured, transmitted to the receptive organ and transduced into electrical signals suitable for the processing by the nervous system. Auditory receptors, hair cells, are tonotopically organized along the basilar membrane, and the distance from the cochlear apex is proportional to the logarithm of the best frequency (Hudspeth, 2000a and 2000b). Information from hair cells is transmitted to neuronal cells from the spiral ganglion. The number of active neurons in the spiral ganglion and their firing rate encode the information about sound intensity. Sound frequency is coded by a “place code” represented by a tonotopic map, which retains in all specific auditory structures including cortical, and a “frequency code”, necessary because tonotopic maps do not contain neurons with a characteristic frequency below 200 Hz. The intermediate frequency (up to about 4 kHz) is encoded by both tonotopy and phase locking represented in a pooled activity of several neurons. At very high frequencies, tonotopy is the main factor for frequency encoding (Hudspeth, 2000a; Bear et al., 2001).

Axons of spiral ganglion neurons contribute to the VIII vestibulo-cochlear cranial nerve. The auditory part of this nerve transmits information to the ipsilateral cochlear nuclear complex situated in the medullo-pontine junction and consisted of three tonotopically organized main parts: dorsal, anteroventral and posteroventral nuclei. The neurons of the cochlear nuclei respond either tonically (and may take part in the frequency encoding) or phasically (cells which fire a single spike to the stimulus onset; they are thought to provide accurate information about the timing of acoustic stimuli and hence take part in sound localization in the horizontal plane). Cells which respond to a broad frequency range are suggested to play role in the localization of sounds along the elevation axis (Altman, 1990; Hudspeth, 2000a; Bear et al., 2001).

The efferents of both the anteroventral and posteroventral nuclei contribute to the trapezoid body, which terminates at the pontine level in the complex of the superior olives. Receiving both ipsi- and contralateral inputs, the medial and lateral olives represent the first level of binaural convergence and play an essential role in sound localization using two localization cues: interaural time and intensity differences (ITD and IID). Some superior olivary neurons respond selectively to a certain direction of frequency modulation (Watanabe et al., 1968; Vartanjan, 1978). Furthermore, some olivary neurons were found to synchronize their activity with relatively high modulation frequencies (150 – 200 Hz) of amplitude-modulated sounds (Andreeva and Vasil’ev, 1977).

The efferents from the superior olives extend to the midbrain auditory structure, the inferior colliculi (IC), via the lateral lemniscus. The IC consists of two main components: the multi-layer central nucleus, which receives most of its projections from lower auditory structures, and the dorsal part, which receives both auditory and somato-sensory input. Within the IC there are areas in which axons from different brainstem nuclei converge integrating

information from the lower level (Oliver et al., 1997). The inferior colliculi obviously play an important role in sound localization since this structure contains numerous neurons sensitive to the interaural time and intensity difference (Altman, 1990; Hudspeth, 2000a; Bear et al., 2001). In response to amplitude- or frequency-modulated sounds, inferior collicular neurons are able to synchronize their firing rate with modulation frequency up to 30 – 100 Hz. This synchronization pattern becomes more robust as the stimulus carrier frequency gets closer to the characteristic frequency of a given neuron (Vartanjan, 1978). Such selectivity to particular combinations of complex stimulus parameters may result in an orthogonal representation of timing and spectral information in the IC (Langner and Schreiner, 1988). While the central nucleus is the main origin of cochleotopic projections to the thalamic level, nuclei of the dorsal part constitute multiple diffuse ascending pathways (Andersen et al., 1980; Calford and Aitkin, 1983).

The most prominent pathways connecting midbrain and thalamic auditory structures, the medial geniculate bodies (MGB), are the brachia of inferior colliculi. The principal, or ventral nucleus of MGB is tonotopically organized and receives its main projections from the central nucleus of the inferior colliculus. Neurons within the ventral nucleus are sharply tuned and produce consistent short-latency responses to tones. The medial, or magnocellular nucleus consists of broadly tuned neurons. A significant part of these neurons is multimodal. Neurons of the deep dorsal nucleus have intermediate tuning and latencies. Other MGB compartments receive diffuse inputs from the inferior colliculi and consist of broadly tuned long-latency neurons (Andersen et al., 1980; Calford and Aitkin, 1983).

At the mesencephalic level, there are connections between the MGB and associative thalamic nuclei: dorso-medial (DM), dorso-lateral (DL), postero-lateral (PL) and Pulvinar. These nonspecific thalamic nuclei, in turn, constitute extensive projections to frontal and parietal associative cortical areas. The DM nucleus sends efferents to Brodmann areas 8 – 12 and 45 – 47, the DL and PL nuclei to parietal areas 5 and 7, while the Pulvinar is connected to areas 39 and 40 (Andreeva et al., 1985). It should be emphasized that some auditory information circumvents the primary auditory cortex and is transferred directly to polymodal areas. However, the main MGB efferents project tonotopically through the acoustic radiation to the primary auditory cortex.

The human primary auditory cortex occupies a part of the transverse gyrus of Heschl on the supratemporal plane and corresponds to Brodmann's area 41 (Morosan et al., 2001). Results from anatomical studies indicate that the human auditory cortex consists of several architectonically defined areas, and at least some of them are suggested to be tonotopically organized (Galaburda and Sanides, 1980; River and Clarke, 1997). Results from a recent fMRI study (Hall et al., 2003) in which multiple frequency-dependent volumes were localized suggested the existence of at least four tonotopically organized areas within the human auditory cortex, of which two were proposed to represent mirror-image maps on Heschl's gyrus. Two mirror-symmetric frequency gradients within Heschl's region were also described in the study by Wessinger et al. (2001).

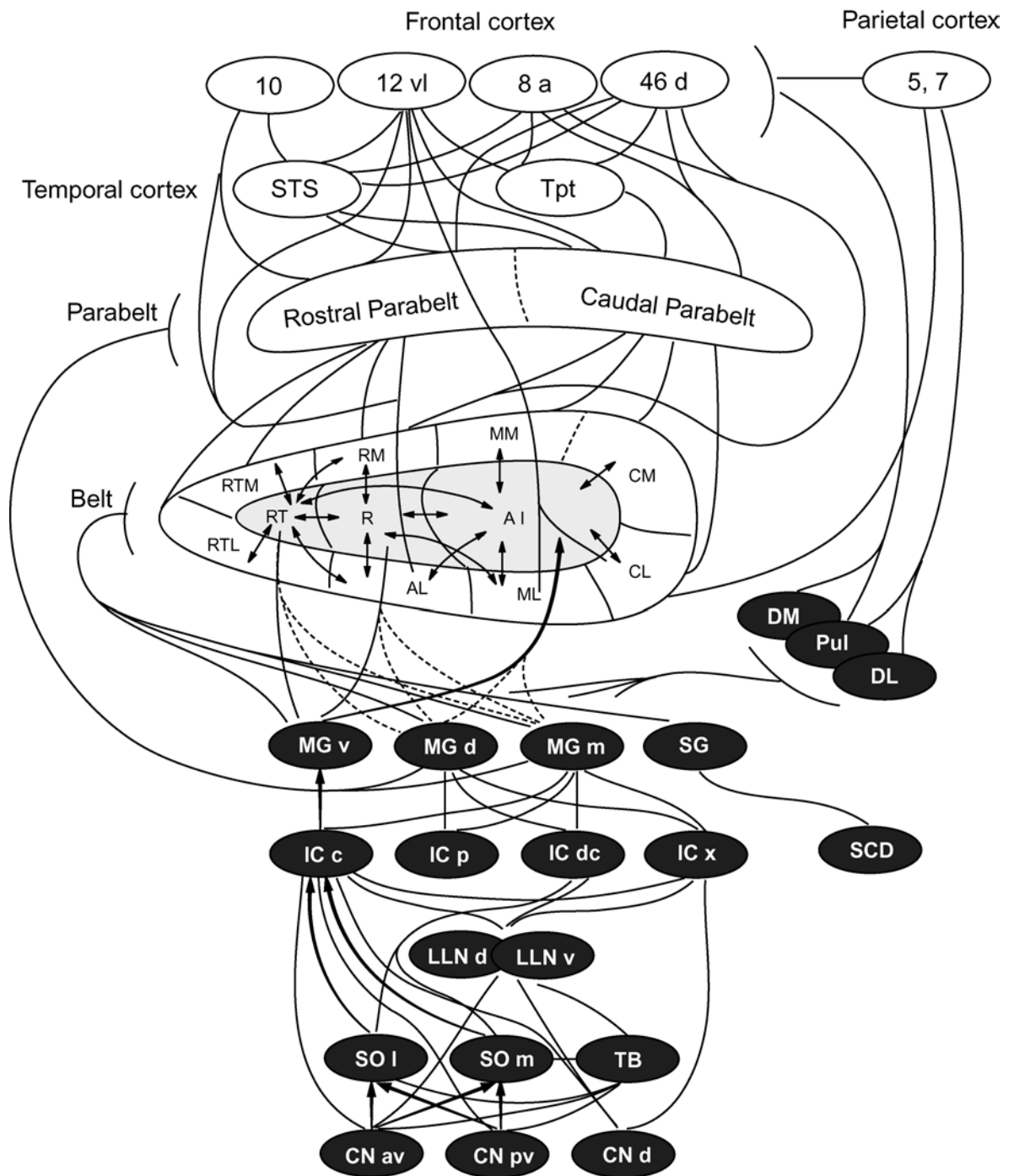


Fig. 2.1.1. Cortical and subcortical connections of the primate auditory system. Subcortical nuclei are shown in black: CN_{av}, CN_{pv} and CN_d – anteroventral, posteroventral and dorsal cochlear nuclei; SO_l and SO_m – lateral and medial superior olives; TB – nuclei of trapezoid body; LLN_d and LLN_v – dorsal and ventral nuclei of the lateral lemniscus; IC_c, IC_p, IC_x – central, pericentral and external nuclei of the inferior colliculus; IC_{dc} – dorsal cortex of the inferior colliculus; SCD – deep layers of the superior colliculus; MG_v, MG_d and MG_m – ventral, dorsal and medial nuclei of the medial geniculate complex; SG – supragenulate nucleus; DM and DL – dorsomedial and dorsolateral thalamic nuclei, Pul – pulvinar. Auditory core areas are shown in grey: AI – auditory area I, R and RT – rostral and rostro-temporal areas. Belt areas: CM – caudomedial, CL – caudolateral, ML – middle lateral, AL – anterolateral, RTL – lateral rostrotemporal, RTM – medial rostrotemporal, RM – rostromedial, STS – superior temporal sulcus; Tpt – temporo-parietal area. Frontal areas: 8a – periauricular, 10 – frontal pole, 12vl – ventrolateral, 46d – dorsal principle sulcus. Some connections are extrapolated from the other mammal's data (adapted and modified from Kaas and Hackett, 2000).

Electrophysiological, optical imaging and anatomical studies in nonhuman primates indicate that auditory processing involves at least 15 cortical areas. According to the latest view, auditory processing in the primate cerebral cortex involves four hierarchic levels (Kaas and Hackett, 2000).

The primary auditory cortex of nonhuman primates consists of three core areas: the most caudal AI, more rostral area (R), and rostromedial area (RT) which extends rostrally from R (Fig. 2.1.1). These fields have a mirror-reflected tonotopic organization and possess the characteristic features of the primary sensory cortex, although these features are less clearly pronounced in the RT. Neurons in these areas are sharply tuned and respond with short latencies to pure tones, they receive prominent input from the principal MGB nucleus (MGv) and all of them have architectonic features specific to the primary sensory cortex. In addition to dense afferents from the MGv, core areas receive some input from the medial and dorsal divisions of the MGB (MGm and MGd). Thus “processing in the auditory cortex starts out in a highly parallel manner, with three primary or primary-like fields receiving direct projections from the MGv” (Kaas and Hackett, 1998). Each core area has rich reciprocal connections with the neighboring core member, and the AI has some interconnections with the RT. Furthermore, all core areas project to the adjacent belt areas and are thought to be responsible for their activation. The auditory belt was suggested to be an obligatory second stage of cortical processing, because there are few or no connections between the core and more distant fields. In addition to ipsilateral connections, there are also dense interhemispheric projections via the corpus callosum targeting in tonotopically matched locations of the homologous core area and adjacent belt (Kaas and Hackett, 1998).

The auditory belt consists of 7 or 8 areas immediately surrounding the core (Kaas and Hackett, 2000) (Fig. 2.1.1). Having dense interconnections with the core, the belt areas receive the richest projections from the immediately adjacent portions of the primary cortex. This input pattern provides a possibility for at least some belt areas to retain a crude tonotopy. Results from electrophysiological recordings from the lateral belt demonstrated tonotopic gradients parallel to those in the neighboring core areas (Rauschecker et al., 1995; Rauschecker and Tian, 2004). Neurons in the belt areas are broadly tuned and respond more consistently to narrow-band noise than pure tones (Rauschecker et al., 1995; Rauschecker et al., 1997), suggesting a convergence of inputs from the core neurons sensitive to adjacent frequencies onto belt neurons (Rauschecker et al., 1995; Kaas et al., 1999). Furthermore, neurons in all lateral belt areas respond more vigorously to species-specific vocalizations compared to energy-matched pure tones and even band-pass noise, and some of those neurons respond better to a certain type of vocalizations (Rauschecker et al., 1995). Similarly, lateral belt neurons were shown to respond selectively to frequency sweeps with a particular speed and direction (Rauschecker et al., 1997).

Neurons in the auditory core as well as in the lateral and caudo-medial belt areas may show response selectivity to the spatial location of the sound source (Sovijärvi and Hyvärinen 1974; Ahissar et al., 1992; Recanzone et al. 2000). Generally, most neurons in mammalian auditory cortex are activated by spatial positions in the contralateral and pericentral fields

(Middlebrooks and Pettigrew, 1981; Imig et al., 1990; Rajan et al., 1990), and a greater proportion of the spatially tuned cells are sensitive to stimulus azimuth than elevation (Recanzone et al., 2000). However, the spatial selectivity of single neurons is several times lower than the psychophysical thresholds. Furthermore, the spatial selectivity of cortical neurons was shown to broaden considerably with increasing sound-pressure levels (Brugge et al., 1994 and 1996; Xu et al., 1998). This suggests that localization acuity may be achieved by a population of neurons, and the connectivity among neurons plays an essential role in encoding of stimulus location (Eisenman 1974; Ahissar 1992; Fitzpatrick et al., 1997).

Based on the results from studies in the cat auditory cortex, Middlebrooks (1994) elaborated a hypothesis of a panoramic code for sound location. According to this view, each broadly-tuned auditory cortical neuron can carry information about locations throughout 360° of azimuth, and this information is coded by both the number and timing of spikes within the response patterns (Middlebrooks 1994; Middlebrooks et al., 1998 and 2002; Furukawa et al., 2000; Furukawa and Middlebrooks 2001 and 2002).

Some of the belt areas were shown to be functionally specialized for the processing of spatial and nonspatial auditory information (Rauschecker and Tian, 2000; Tian et al., 2001). Caudal belt neurons are generally more selective for the auditory spatial location, while neurons in the anterior belt have stronger selectivity for sound content (type of monkey vocalization).

Most thalamic afferents to the belt areas originate in the MGm and MGd, while the MGv has only sparse projections to the belt. However, since the neuronal responses in the belt are markedly reduced following lesions of the primary areas (Rauschecker et al., 1997), the belt is suggested to be mostly dependent on core inputs for activation (Kaas and Hackett, 2000). The belt areas are also interconnected with adjacent and more distant areas within the belt. Furthermore, there are connections of the belt with hierarchically higher cortical areas – the parabelt region and frontal lobes (Kaas and Hackett, 2000).

The third level of the auditory processing is represented by the parabelt, located next to the lateral belt region. Having some ascending inputs from the MGm, MGd, supragenulate nucleus, nucleus limitans and pulvinar, the parabelt seems to be more likely dependent on the belt rather than thalamic inputs (Kaas and Hackett, 2000). The parabelt has been divided into the rostral part, which receives main inputs from the rostral belt areas, and the caudal part, largely connected to caudal belt areas. Both rostral and caudal parabelts receive inputs from the rostromedial belt area (Kaas and Hackett, 2000). In addition, the parabelt is interconnected through the corpus callosum with its homologous area in the contralateral hemisphere.

The targets of the parabelt constitute the fourth level of the auditory processing. Projections from parabelt extend to the temporal, parietal and frontal lobes. Within temporal lobes, the parabelt is connected with the associative auditory cortex in the superior temporal gyrus, and polymodal cortex in the superior temporal sulcus. The parabelt also has some connections with the temporo-parietal area (Tpt). In the study by Leinonen et al. (1980), neuronal responses in the Tpt were shown to depend on the presentation location of the sound with reference to the monkey's head.

In the parietal lobe, the parabelt targets area 7a involved in guiding reach. In the frontal lobes, the parabelt projects to the frontal eye field (area 8a) responsible for directing the gaze towards the object of interest, dorsolateral (area 46) and ventrolateral (area 12) prefrontal cortex involved in different types of working memory tasks, and, finally, to orbito-frontal cortex associated with the reward system, emotions and motivations.

In conclusion, it is important to stress that the caudal fields of the nonprimary auditory cortex preferably target the spatial domains in the prefrontal cortex (e.g., areas 8a, caudal 46), while the more rostral fields are stronger interconnected with nonspatial regions (e.g., areas 10, 12, rostral 46) (Petrides and Pandya, 1988; Romanski et al., 1999; Hackett et al., 1999). Thus, auditory processing involves multiple parallel streams, which may have different functional roles. However, dense interconnections within each processing level suggest a considerable cross-talk across those streams (Kaas and Hackett, 1998; Kaas and Hackett, 2000).

2.2. Processing of spatial and nonspatial auditory information

2.2.1. Processing of spectro-temporal characteristics

2.2.1.1. Frequency

Results from several PET and fMRI studies suggest that the location of activated volume within the temporal lobes depends on sound frequency (Lauter et al., 1985; Wessinger et al., 1997; Bilecen et al., 1998; Talavage et al., 2000; Yang et al., 2000; Wessinger et al., 2001; Hall et al., 2003), which reflects underlying tonotopic organization of the auditory cortex.

Results from lesion studies suggest that simple frequency discrimination can be accomplished at subcortical level. Unilateral (Zatorre, 1988; Zatorre and Samson, 1991) or even large bilateral lesions of the auditory cortices (Peretz et al., 1994) do not generally result in a permanent impairment in frequency discrimination tests.

In normal subjects, perception of sound frequency was shown to elicit asymmetrical activation of the temporal cortex favoring the right hemisphere (Tzourio et al., 1997). Auditory attention to tone frequency enhanced the activity in the auditory areas of the superior temporal cortex predominantly in the hemisphere contralateral to the attended direction (Tzourio et al., 1997; Alho et al., 1999), and in the prefrontal (Tzourio et al., 1997; Jäncke et al., 1998; Alho et al., 1999) and parietal (Zatorre et al., 1999; Stevens et al., 2000) cortical areas, which appear to be involved in controlling attention (Tzourio et al., 1997; Alho et al., 1999). Activation within the parietal cortex had an earlier onset than activation in the prefrontal areas (Stevens et al., 2000). Thus, two networks are involved during selective attention to sound frequency: a local temporal network, responsible for the perceptual analysis of frequency and a fronto-parietal network modulating temporal cortex activity and its functional lateralization: a decrease of general rightward dominance and appearance of lateralization dependent on the side of attended stimulation (Tzourio et al., 1997).

2.2.1.2. Intensity

Sound intensity has been shown to increase activation volume within the auditory cortex (Bilecen et al., 2002; Brechmann et al., 2002), especially within the primary auditory areas (Hart et al., 2002). Furthermore, there is evidence of the existence of an amplitopic pattern of intensity encoding (Bilecen et al., 2002). The activated areas moved in the dorso-medial direction along the HG with increasing sound pressure level (SPL). This finding is consistent with the results from single-cell recordings from the primary auditory cortex (Heil et al., 1994; Phillips et al., 1994) and a MEG study by Pantev et al. (1989) showing an amplitopic gradient perpendicular to the tonotopic gradient. Selective attention to sound intensity, activated right STG, right parietal and frontal areas (Belin et al., 1998). Activity in the right temporal cortex was independent of discrimination difficulty, suggesting selective involvement of this area in the sensory aspects of the detection of intensity changes. This observation is consistent with patient data showing that unilateral excision of the right temporal lobe (Milner, 1962) may cause deficits in intensity discrimination. Activity within the right-hemispheric fronto-parietal network, conversely, was modulated by the attentional demands – it was inversely proportional to intensity discriminability. Thus, discrimination of sound intensity involves two different cortical networks: a right fronto-parietal network responsible for allocation of attention, and a region of the associative auditory cortex specifically involved in sensory computation of sound intensity differences (Belin et al., 1998).

On the other hand, intensity discrimination ability may be preserved (Engelien et al., 1995) or slightly reduced (Baru, 1978) even after bilateral perisylvian lesions, indicating that intensity coding may to some extent be accomplished by subcortical auditory structures.

2.2.1.3. Duration

Discrimination of sound duration was shown to produce extensive activation within both cortical and subcortical structures (Rao et al., 2001; Belin et al., 2002). Part of the activation pattern, consisting of a set of fronto-parietal zones (frontal operculum, premotor regions and IPL) in the right hemisphere, was very similar to the pattern observed during sound intensity discrimination (Belin et al., 1998) and the discrimination of duration or intensity of a visual stimulus (Maquet et al., 1996), suggesting that the right fronto-parietal network could be activated in attentional tasks irrespective of the sensory modality or the stimulus attribute being attended to (Belin et al., 2002). Activation, related to the processing of sound duration *per se*, was observed in the right orbital prefrontal cortex, right thalamus, right basal ganglia (putamen and caudate nucleus), right MTG and cerebellum (Belin et al., 2002). In an event-related fMRI study by Rao et al. (2001), investigating the evolution of brain activation during temporal processing, early activation observed in the basal ganglia was interpreted to be associated with the encoding of time intervals, whereas the later activation in the right dorsolateral prefrontal cortex was proposed to reflect the comparison of time intervals.

Lateral parts of the cerebellum have been shown to play a critical role in timing operations (Ivry, 1996; Ivry and Spencer, 2004). The involvement of the right prefrontal cortex

in temporal tasks was also indicated by the results from lesion (Harrington et al., 1998) and other neuroimaging (Pedersen et al., 2000; Pouthas et al., 2000) studies.

Observations in brain-damaged patients generally suggest left-hemispheric specialization for auditory temporal processing (Swisher and Hirsh, 1972; Robinson and Solomon 1974; Prior et al., 1990; Robin et al., 1990). However, some data argue against lateralization. For example, patients with right hemispheric lesions including Heschl's gyrus were impaired in an auditory but not a visual rhythm reproduction task. Such deficits may indicate the importance of the right temporal lobe, and particularly the right HG, in the generation or retention of an accurate auditory image, which could be specific to sound duration but might also include pitch (Penhune et al., 1999).

Thus, the above results suggest that the discrimination of sound duration is performed by two cortical networks: a supramodal right fronto-parietal network and a network including the basal ganglia, temporal lobes, cerebellum and right prefrontal cortex, more specifically involved in auditory temporal processing.

2.2.1.4. Stimulus complexity

While pure tone stimuli generally result in small, restricted foci of activation, band-pass noise produces larger, more extensive regions of activation (Wessinger et al., 2001). Harmonic tones produce more activation than single tones in the right HG and bilaterally in the supratemporal plane (Hall et al., 2002). Perception of spectral motion, a critical component of music (frequency modulation) and speech (formant transition), was shown to activate selectively areas distinct from the primary auditory cortex bilaterally in the STG and STS (Hall et al., 2002; Thivard et al., 2000).

Within the supratemporal plane, the regions activated both by pure tones and complex sounds are surrounded by regions that respond only to complex sounds, providing evidence for the same basic organizational pattern for both humans and monkeys. Similarly, areas surrounding the HG bilaterally, particularly the planum temporale (PT) and dorsolateral STG, were more strongly activated by FM-tones than noise, suggesting a role of these areas in the processing of simple temporally encoded auditory information (Binder et al., 2004). This hierarchical system was suggested to participate in the early processing of a broad variety of complex sounds, including human speech.

In a selective attention study, dichotically presented environmental and speech sounds, similarly to tones (Alho et al., 1999), caused asymmetric activation in the temporal lobes, resulting in an increase of the cerebral blood flow in the hemisphere contralateral to the attended ear and a decrease in the opposite hemisphere (O'Leary et al., 1996) and the involvement of frontal network, including the anterior cingulum, and the precentral and right dorso-lateral prefrontal cortices, that could mediate the temporal cortex modulation by selective attention. Discrimination between rising and falling FM tones (Pugh et al., 1996) or between syllables (Pugh et al., 1996; Benedict et al., 1998) resulted in activation of the superior and middle temporal cortex, prefrontal areas, and inferior and superior parietal lobes. Increasing attentional demands from a binaural to a dichotic condition for both pitch and

speech judgments resulted in enhanced activation within bilateral temporal as well as parietal and frontal areas, preferentially in the right hemisphere. Increases in the IFG and MTG activations from the binaural to the dichotic condition were stronger in the left hemisphere for speech and in the right hemisphere for pitch judgments (Pugh et al., 1996).

2.2.1.5. Temporal regularity

The temporal characteristics of sound were suggested to be processed hierarchically in the auditory system (Griffiths et al., 1998a). Activity in the primary auditory cortex was shown to vary as a function of temporal regularity of stimuli, whereas the auditory associative cortex, bilaterally in the anterior temporal lobes and in the posterior superior temporal gyri, was sensitive to long-term pitch changes in the range of music and speech. These findings indicate that the auditory structures up to the level of the primary auditory cortex are involved in the analysis of the fine temporal structure of auditory stimuli, while the analysis of pitch sequences takes place at a higher anatomical level in the associative auditory cortex.

Results from another study by the same group (Griffiths et al., 2001) demonstrated that the processing of temporal regularity in the auditory ascending pathway begins as early as at the level of the CN. The parametric analysis revealed that activation of CN and IC bilaterally and in the right MGB increased with the level of temporal regularity. Furthermore, the IC has been shown to be more sensitive to temporal regularity than the CN. However, long-term alteration in stimulus pitch did not produce changes in activity either in the brainstem or within the primary auditory cortex. In contrast, secondary auditory areas including the lateral HG and PT were sensitive to long-term signal changes.

In an fMRI study by Giraud et al. (2000), several auditory structures were shown to be specifically involved in the processing of amplitude-modulated (AM) sounds: the lower brainstem (SOC), the IC, the MGB, Heschl's gyrus, the STG, the STS and the IPL. The subcortical and cortical structures within the auditory pathway responded preferentially to particular AM frequencies: the lower brainstem to 256 Hz, the IC to 32 – 256 Hz, the MGB to 16 Hz, the primary auditory cortex to 8 Hz and secondary regions to 4 – 8 Hz, suggesting that “the human auditory system is organized as a hierarchical filter bank, where each level of the auditory pathway could be considered as a filter in the AM domain with a best frequency that decreases from the periphery to the cortex”. Similar results were obtained in another fMRI study by Harms and Melcher (2002), focusing on the effect of the sound repetition rate on hemodynamic responses of structures along the auditory pathway. Trains of noise bursts elicited responses in the IC, which gradually increased with repetition rate up to 35 Hz. The maximal response in the MGB was observed at 20 Hz. In primary cortical areas within the HG, the greatest activation occurred at the stimulation rate of 10 Hz, and finally, in the STG the greatest averaged percent change was observed at 2 Hz. Importantly, the peak of the time-averaged activation at repetition rates around 8 Hz was similarly observed for the visual (Thomas and Menon, 1998; Zhu et al., 1998) and somatosensory (Takanashi et al., 2001) modalities, and appears to represent a general property of the primary sensory areas (Harms and Melcher, 2002).

These results are consistent with electrophysiological studies showing a similar bottom-up inverse gradient in the preferential responses of neurons in the auditory structures to different AM frequencies (Andreeva and Vasil'ev, 1977; Schreiner and Urbas, 1986 and 1988; Langner and Schreiner, 1988; Heil and Irvine, 1998; Kuwada and Batra, 1999). A set of lesion studies in rats (Grigor'eva and Vasil'ev, 1981a,b; Grigor'eva et al., 1987; Grigor'eva et al., 1988; Vasil'ev et al., 1988) also provide support for the hierarchical filter bank organization of the auditory system. The authors performed bilateral ablations of the auditory cortex and subcortical nuclei in rats trained to discriminate pure tones from AM-tones with the same carrier frequency. Results demonstrated that the auditory cortex was crucial for the processing of AM frequencies below 30 Hz, IC – below 180 Hz, whereas the processing of higher AM frequencies was accomplished by the SO complex.

In summary, the perception of auditory nonspatial features involves both primary and associative auditory areas. Selective attention to different sound attributes additionally activate a supramodal fronto-parietal network, which is suggested to produce a modulatory effect on local temporal networks. Finally, retention of auditory nonspatial information in working memory is accomplished by associative frontal, parietal and temporal cortical areas beyond perceptual analysis (Zatorre et al., 1994; Weeks et al., 1999; Lewis et al., 2000; Alain et al., 2001).

2.2.2. Processing of auditory spatial information

2.2.2.1. Localization of stationary sounds

The ability to localize sounds plays a critical role in survival. The distance between the two ears and the shadowing effects of the head and pinnae produce several interaural disparities such as a transient arrival time, differences in the on-going phase, intensity and spectral characteristics of the sound. Combination of these parameters provides quite precise information about the spatial location of a particular sound source. While spectral cues are especially effective for sound localization in the vertical plane, they also may contribute to the estimation of azimuth. However, for the precise localization in the horizontal plane, interaural time and intensity differences (ITD and IID) are the most reliable sources of information. Humans are able to distinguish interaural delays at the range of 10 μ s and locate the sound sources with an accuracy of few degrees. The ITD is essential for the localization of low-frequency sounds (lower than 1500 Hz), when the length of the sound cycle is greater than the interaural distance. For high-frequency sounds the IID cue becomes preferential. For low-frequency sounds, in turn, this cue is not so informative because long sound waves diffract around the head and the interaural intensity difference is relatively small (Trimble, 1929 and 1935).

When no active task performance is required, variation in the sound source location was shown to produce specific activation within the auditory cortex: caudo-medial portions of planum temporale, lateral HG and planum polare. In contrast, variation in sound pitch activated

antero-lateral portions of the PT (Warren and Griffiths, 2003) suggesting dissociation between the processing of spatial and nonspatial sound features as early as at the perceptual level. Furthermore, activity within the posterior auditory areas extending in the left hemisphere to the temporo-parietal operculum was shown to co-vary with the spatial distribution of simultaneously presented environmental sounds (Zatorre et al., 2002). Active localization tasks consistently involve the right inferior parietal cortex (Bushara et al., 1999; Weeks et al., 1999; Zatorre et al., 2002). In addition, auditory localization may involve the right superior parietal lobe (Bushara et al., 1999), right (Zatorre et al., 2002) or bilateral (Bushara et al., 1999) prefrontal cortex, right medial temporal gyrus (Bushara et al., 1999) and motor-related structures (Bushara et al., 1999; Weeks et al., 1999; Zatorre et al., 2002). However, activation of the motor-related structures observed in all three above-mentioned studies appears to be non-specific to the auditory localization *per se* and caused by passive listening or rest baseline conditions, while, in contrast, activation of the right IPL remained significant when baseline included sham motor responses (Zatorre et al., 2002). Selective attention to sound location was shown to activate a fronto-parietal network similar to that observed in the other studies concerning the effects of selective attention to different sound attributes (Zatorre et al., 1999).

Working memory processing of sound source location was shown to involve the right (Bushara et al., 1999) or bilateral (Martinkauppi et al., 2000; Alain et al., 2001) associative auditory cortices, bilateral superior (Bushara et al., 1999; Martinkauppi et al., 2000) and/or inferior parietal lobes (Bushara et al., 1999; Weeks et al., 1999; Martinkauppi et al., 2000) as well as dorsal (Weeks et al., 1999; Martinkauppi et al., 2000; Alain et al., 2001; Zatorre et al., 2002) and ventral (Martinkauppi et al., 2000; Maeder et al., 2001) prefrontal areas with right-hemispheric dominance.

Results of direct comparisons between spatial and nonspatial tasks have consistently demonstrated that working memory processing of sound location activates more strongly the inferior parietal lobes bilaterally (Alain et al., 2001; Maeder et al., 2001) or only in the right hemisphere (Weeks et al., 1999). Non-spatial tasks, on the other hand, preferentially activated the associative auditory cortex in the superior or inferior temporal gyri (Alain et al., 2001; Maeder et al., 2001). Furthermore, subareal segregation between spatial and nonspatial working memory processing was found within the associative cortex. Spatial tasks were shown to involve more lateral areas within the parietal lobes (Lewis et al., 2000), more posterior within the temporal (Alain et al., 2001) and more superior within the prefrontal cortex (Alain et al., 2001; Maeder et al., 2001). Thus it is feasible to conclude that the processing of auditory spatial information preferentially involves the posterior temporo-parietal pathway, whereas nonspatial information is processed along the ventral pathway that involves anterior temporal and inferior frontal areas.

A recent meta-analysis study by Arnott et al. (2004) also supported the dual-stream model for auditory information processing in the human brain. Their results demonstrated that activation of the IPL was reported in 10 out of 11 spatial studies as compared to 41% of nonspatial studies. Activity around the SFS was found in 55% of spatial and only in 7% of nonspatial studies, while inferior frontal activity, in contrast, was reported in 56% of nonspatial

and in 9% of spatial studies. Finally, spatial tasks activated mainly posterior temporal areas, while the activity related to nonspatial tasks was widely distributed throughout the temporal lobes.

More evidence supporting the dual-stream model has been obtained from clinical studies in brain-damaged patients. The double-dissociation between spatial and non-spatial auditory processing was observed in the study by Clarke et al. (2002). The authors reported selective deficits in sound localization ability, when the lesions involved the inferior parietal and frontal cortices and the STG, or in sound recognition when the lesion affected the temporal pole, and the inferior and middle temporal gyri. However, according to another case report, a patient with a right hemispheric lesion including the IPL, STG, AG, inferior and middle frontal gyri, and insula suffered from auditory agnosia, demonstrated deficits in pitch discrimination, but had a normal sound localization ability (Spreeen et al., 1965).

In general, the results from clinical observations in human patients with brain lesions are highly contradictory, which may be due to differences in the size, location or etiology of the lesions. However, even when these factors are taken in account, there is still a considerable inconsistency among the data. For example, focal unilateral lesions may result in selective deficits in sound localization, as it was observed in the study by Clarke et al. (2000). On the other hand, patients can demonstrate some preservation of localization ability of either stationary (Zatorre et al., 1995) or moving sounds (Lessard et al., 1999) even after complete hemispherectomy. Unilateral temporal lobe lesions were shown to cause impairment in the ability to localize sounds in the auditory hemifield contralateral to the lesion (Sanchez-Longo and Forster, 1958; Klingon and Bontecou, 1966). However, in other studies in patients with unilateral temporal lobe lesions, localization deficits have not been observed (Shankweiler, 1961; Gazzaniga et al., 1973). Bilateral temporal lobe lesions were found to result in a severely impaired (Klingon and Bontecou, 1966; Albert et al., 1972; Michel and Peronnet, 1980; Engelen 1995) or almost normal sound localizing ability (Jerger et al., 1972; Kanshepolsky et al., 1973). Sanchez-Longo and Forster (1958) emphasized the role of the temporal lobes in auditory spatial processing. He found that only lesions involving the temporal lobes produced deficits in sound localization in the contralateral auditory field. Klingon and Bontecou (1966) on the basis of observations of big group of patients argued against that auditory localization could be ascribed to a specific lobe. Among 33 patients who demonstrated localization deficits, some had lesions involving either parietal or temporal, occipital and frontal lobes contralateral to the side of the localization deficit.

Data concerning hemispheric specialization for auditory spatial processing are also contradictory. Altman et al. (1987) demonstrated that subjects with right but not left unilateral damage of the temporal cortex were impaired in perceiving the length of a simulated movement trajectory, suggesting that the right hemisphere contributes more than the left to the analysis of spatial auditory characteristics. Results of the study by Pavani et al. (2002) indicated the role of right IPL in auditory spatial processing along elevation axes. Similarly, a right-hemispheric lesion involving parietal cortex caused impairment in sound movement detection (Griffiths, 1996 and 1997). On the other hand, Pinek et al. (1989) suggested a

particular role of the left parietal lobe in sound localization. Subjects with left hemispheric unilateral parietal lobe damage had very large localization deficits in both the horizontal and vertical dimensions of both auditory hemifields, whereas right-hemispheric patients had localization deficits only in the horizontal plane in the periphery of the left auditory field. Finally, in the study by Clarke et al. (2000), sound localization was shown to depend on processing in either hemisphere, although right hemispheric lesions appeared to yield greater deficits which could involve the whole space, while left hemispheric lesions were found to involve mainly the right hemisphere.

Thus, it seems possible to conclude that processing of spatial location of stationary sounds may involve brain structures beyond the auditory cortex, presumably in the parietal lobes.

2.2.2.2. Processing of sound motion

While location of stationary sound is estimated on the basis of the three localization cues, continuous temporal variation of these cues contributes to the perception of the direction and velocity of sound motion.

The first neuroimaging study of sound motion processing was conducted by Griffiths et al. using PET (1994). Binaural stimulation simulating sound movement within the head selectively activated a right-hemispheric network including the insula, posterior cingulate cortex and cerebellum. The insular cortex was suggested to be an auditory analog to the visual motion area. In a later study Griffiths and colleagues (1998b) demonstrated that the right superior parietal area has an essential role of in the perception of auditory motion. An additional bilateral fronto-parietal network activated in the fMRI experiment was attributed to the increase of attentional demands due to the background noise of the fMRI scanner. However, the involvement of a bilateral fronto-parietal network in sound motion processing was confirmed in further experiments employing auditory stimuli moving along both the horizontal and vertical axes (Pavani et al., 2002) as well as rotating stimuli (Griffiths and Green, 1999; Warren et al., 2002). Furthermore, areas within the frontal and parietal cortices were commonly activated by auditory, visual and tactile motion (Lewis et al., 2000; Bremmer et al., 2001).

In a study by Baumgart et al. (1999) moving vs. stationary sounds activated exclusively the right PT, which has been interpreted to be the missing link between the primary auditory cortex and presumably associative parietal areas. However, the authors used a limited number of imaged slices, which made it impossible to detect activation in the frontal and parietal areas.

The results from lesion studies (Yamada et al., 1996 and 1997) demonstrated that patients with either bilateral or unilateral temporal lobe lesions could discriminate the direction of moving sound created on the basis of IID variation, although the sensitivity to discriminate IID was reduced when the auditory cortex was damaged. On the other hand, all patients with unilateral but none with bilateral lesions could discriminate the direction of moving sound when the variation of the ITD cue was used to produce the illusion of sound motion. ITD thresholds were significantly higher in patients than control subjects. The results suggest that at

least one spared auditory cortex is necessary for the detection of ITD, whereas the role of the auditory cortex may not be essential in discriminating IID. A more extensive unilateral lesion involving the supero-posterior temporal lobe, parietal cortex and insula in the right hemisphere was shown to cause deficits in detection of sound movement regardless of whether it was defined by phase or loudness cues (Griffiths et al., 1996 and 1997).

Thus, processing sound motion appears to involve both primary auditory and associative areas within the temporal (the PT), frontal, and parietal lobes.

In summary, there is some indication that the processing of spatial and nonspatial auditory information may be dissociated already at the perceptual level within the supratemporal plane. Selective attention to different sound attributes involves a relatively similar non-specific fronto-parietal network, which has been suggested to modulate temporal cortex activity and its functional lateralization. However, further increase of cognitive demands, like in working memory tasks, may produce task-related segregation within associative neuronal networks, with spatial tasks involving more strongly parietal and superior frontal areas and nonspatial tasks preferentially activating anterior temporal and inferior frontal areas. Furthermore, it has been suggested that within the prefrontal cortex, the mnemonic processing is domain-specific (Goldman-Rakic, 1994 and 1995). This domain-specific model was proposed for the visual information processing on the basis of several lesion and electrophysiological studies in non-human primates, however it meets some support for the auditory modality as well (Petrides and Pandya, 1988; Hackett et al., 1999; Romanski et al., 1999).

However, this review would be incomplete without mentioning an alternative hypothesis proposed by Petrides (1994). According to this hypothesis working memory processes in the dorsolateral and ventrolateral frontal cortical areas are organized relative to the nature of the processing required rather than to the domain of the information to be remembered. This hypothesis has gained support from several studies on the visual modality (for review see Owen, 2000) and from an auditory verbal study by Owen et al. (2000). Activation in ventrolateral regions was generally observed in tasks in which behavioral responses were based on the information simply stored in the working memory buffer (e.g., delayed matching-to-sample), whereas dorsolateral (particularly mid-dorsolateral) regions were involved in tasks requiring active manipulation or continuous updating of the on-going record (e.g., n-back task). In a study by Martinkauppi et al. (2000) employing a parametric design, bilateral activation of the mid-dorsolateral prefrontal cortex was observed in subtractions of 1-back from 3-back auditory spatial tasks. On the other hand, activation in the mid-dorsolateral prefrontal cortex was documented in simple auditory selective attention (Pugh et al., 1996; Jäncke et al., 1998; Alho et al., 1999; Zatorre et al., 1999; Belin et al., 2002) and matching-to-sample tasks (Bushara et al., 1999). When compared to visual tasks with the same load, auditory tasks are usually perceived as more difficult (e.g., Martinkauppi et al., 2000) and may therefore produce activation in mid-dorsolateral regions even during relatively simple tasks. However, an increase in cognitive demands, such as a higher memory load, selective interference, or the requirement to rearrange the order of memory items, generally produce

more consistent and extensive dorso-lateral activation (Zatorre et al., 1994; Martinkauppi et al., 2000; Owen et al., 2000). In conclusion, it is important to mention that the discussed model does not rule out the possibility for functional segregation between attribute-specific processing (spatial vs. nonspatial) within frontal areas (Owen, 2000).

2.3. Auditory long-latency evoked responses

According to the predominant classification (Donchin et al., 1978), components of event-related potentials (ERP) can be categorized as exogenous or endogenous. Exogenous components are mainly determined by external stimulus characteristics, whereas endogenous components are more variable and flexible and only partially depend on physical stimulus parameters being determined rather by stimulus relevance and subject's intentions. ERP components can also be classified on the basis of their temporal characteristics into early, middle- and long-latency (late). While early and middle-latency responses are known to be fully exogenous, late responses may share exogenous and endogenous features or be fully endogenous.

Long-latency components of auditory evoked potentials include the prominent negative wave, N1, which peaks at around 100 ms, and the consecutive positivity, P2, with a latency of about 160-200 ms. According to Hyde (1997), the N1 and P2 occupy a "grey zone", having both exogenous and endogenous features. On one hand, they are strongly affected by physical stimulus variables and, on the other hand, by attentional demands (Hillyard et al., 1973; Hillyard, 1981; Woldorff, 1995). The following N2 and P3 components are thought to represent mainly endogenous responses.

2.3.1. N1

First described by Davis in 1939 as a "vertex potential", the N1 is now in the focus of interest in the ERP research as the most prominent and stable transient response. The N1 is elicited by stimulus onset and offset, if the sound's duration exceeds 500 ms (Davis and Zerlin, 1966). The offset response is usually smaller and has a shorter latency than the onset response (Onishi and Davis, 1968). Their scalp distributions are rather similar (Picton et al., 1978a; Näätänen and Picton, 1987), but generators may be partially different (Hari et al., 1987). The N1 can also be evoked by a change in the frequency or intensity of a continuous sound (Arlinger et al., 1982; Lavikainen et al., 1995). An increase of the stimulus duration enhances both the onset (but only up to 30-50 ms) (Kodera et al., 1979) and offset responses (Lü et al., 1992), whereas the prolongation of the rise-fall time, conversely, decreases the N1 amplitude (Onishi and Davis, 1968; Kodera et al., 1979).

The N1 becomes more prominent and its latency shortens with increasing stimulus intensity (Beagley and Knight, 1967), however, very high intensities may saturate or even reduce the amplitude of N1 (Picton et al., 1970; Buchsbaum, 1976). At very low, near-threshold intensities, the N1 becomes a small broad wave with a latency around 150-200 ms (Parasuraman et al., 1982), and was suggested to be overlapped with the consecutive negative

wave, the N2 (Näätänen and Picton, 1987). The tonal frequency alters the N1 amplitude considerably: the N1 decreases when the frequency increases, especially at frequencies higher than 2000 Hz (Antinoro and Skinner, 1968; Picton et al., 1978b). The N1, even when dramatically reduced, can be reliably detected up to a stimulus frequency of 14 kHz, at 15 kHz it is absent in some of subjects, and no N1 can be detected at 20 kHz (Fujioka et al., 2002). The authors suggested that the amplitude reduction at high frequencies might be due to the receptive fields in the auditory cortex being small for less useful sounds. The latency of the N1 was observed to vary parabolically with tonal frequency: it decreased with increasing tonal frequency from 100 to 500-1000 Hz. A further frequency increase was associated with gradual latency prolongation (Roberts and Poeppel, 1996; Roberts et al., 2001; Lüthenhöner et al., 2003).

The amplitude of the both electric and magnetic counterparts of the N1 was shown to be attenuated by repeatedly presented stimuli, with the amplitude decrease being stronger when the ISI was shorter (Milner, 1969; Rothman et al., 1970; Fruhstorfer et al., 1970 and 1971; Picton et al., 1977; Hari et al., 1982; Woods and Elmasian, 1986; Budd et al., 1998; Onitsuka et al., 2000; Sörös et al., 2001). The asymptotic level of the amplitude may be reached already at the second or third stimulus in the train (Fruhstorfer et al., 1970; Woods and Elmasian, 1986; Bourbon et al., 1987; Lammertmann et al., 2001; Sörös et al., 2001). The amplitude of the N1 saturates at shorter ISIs when the stimuli are of low intensity (Picton et al., 1970; Nelson and Lassman, 1973). There are also reports of prolongation of the N1 latency under repeated stimulation (Onitsuka et al., 2000; Sörös et al., 2001). The stimulus repetition rate was shown to affect differently the magnetic and electric counterparts of the N1: the N1m saturated at shorter ISIs than the N1, suggesting an additional generator contributing to the electrical vertex response (Hari et al., 1982). The N1 response to an auditory stimulus may be attenuated if it is preceded by stimulus of another modality (Fruhstorfer, 1971; McLean et al., 1975). These generalized effects suggest the presence of a non-specific source contributing to the generation of the N1 (Näätänen and Picton, 1987).

In contrast to the intermodal effects on the N1, this response can demonstrate high stimulus specificity. When intervening tones were inserted in a train of repetitive test tones, the amplitude of the N1 elicited by the test stimuli increased as a function of the frequency separation between the test and intervening tones (Butler, 1968; Picton et al., 1978a; Näätänen et al., 1988). In the latter study, the frequency of the equiprobable intervening stimuli varied in parallel with their spatial location along the horizontal dimension. The amplitude of the N1 elicited by the test stimuli was smaller the smaller was the separation between the test and intervening stimuli in frequency or location. Furthermore, the frequency and location effects were independent suggesting separate detectors for frequency and location of an auditory stimulus (Näätänen et al., 1988).

In addition to short-term habituation across a train of several repetitive sounds, long-term habituation of the N1 and N1m amplitude has been demonstrated over the first 10-30 minutes of stimulation (Woods and Elmasian, 1986; Polich et al., 1988; Rosburg et al., 2002).

Under monaural stimulation, both the electric and magnetic N1 usually have higher amplitude and shorter latency in the hemisphere contralateral to the stimulation (Vaughan and Ritter, 1970; Knight et al., 1980; Giard et al., 1994; Lavikainen et al., 1994; Nakasato et al., 1995; Pantev et al., 1998; Virtanen et al., 1998; Picton et al., 1999). Sounds presented binaurally, elicited stronger and/or earlier N1 responses over the right than left hemisphere, suggesting right hemispheric dominance in the processing of non-verbal auditory information (Kanno et al., 1996; Yvert et al., 1998; Roberts et al., 2001; Fujioka et al., 2002), whereas processing of speech sounds may enhance the N1 over the left hemisphere (Morrell and Salamy, 1971; Wood et al., 1971).

There is no agreement concerning the effect of binaural interaction on the N1. The amplitude of the N1 was shown to be slightly increased by binaural compared to monaural stimulation (Picton et al., 1978b); this increase was, however, much smaller than might be expected from the addition of two monaural responses (Näätänen and Picton, 1987). In some other studies, the N1 was clearly suppressed by binaural stimulation (Pantev et al., 1986; Lavikainen et al., 1997; Yvert et al., 1998). These data suggest mutual inhibition between the populations of neurons involved in the generation of the N1 (Näätänen and Picton, 1987; Altman and Vaitulevich, 1992).

Internal factors may also modulate the N1. In healthy subjects the N1 is considerably reduced during sleep (Picton et al., 1974; Paavilainen et al., 1987). In wakefulness the most robust effect on the N1 is produced by attention. However, besides the view that attention modulates the neural generators of the N1 (Woldorff, 1995), it has been suggested that the effect of attention can be dissociated from the “true” N1 and causes the superimposition on the N1 of the endogenous processing negativity (Näätänen and Picton, 1987; Näätänen, 1992).

Different methodological approaches have been employed for the analysis of generators of the N1 component. Lesion studies have provided rather contradictory results. After bilateral temporal lobe lesions, long-latency auditory ERPs may be completely abolished (Jerger et al., 1969; Michel et al., 1980) or practically non-affected (Woods et al., 1984). This discrepancy most probably results from different lesion extension. Unilateral temporal lesions have been shown to produce marked asymmetries of long-latency evoked responses (Peronnet et al., 1974; Scherg and von Cramon, 1986). Selective unilateral lesions of the acoustic radiation (auditory cortical areas remained however spared) did not diminish but delayed late activity, probably reflecting indirect activation of the preserved areas by commissural pathways from the undamaged hemisphere. When lesions involved both the primary and associative auditory cortices, long-latency auditory evoked potentials were abolished in the damaged hemisphere (Scherg and von Cramon, 1986). Temporo-parietal lesions dramatically and symmetrically reduced the N1, while frontal lesions did not significantly alter the overall amplitude or latency of this peak (Knight et al., 1980). However, when the site of the lesion and the ear of stimulation in the frontal-damaged group were considered together, the N1 was found to enhance in response to the stimulation contralateral to the damaged hemisphere (Knight et al., 1980), leading the authors to suggest an inhibitory modulatory function for the frontal cortex. The symmetric reduction of the N1 following unilateral temporo-parietal lesions contradicts

the suggestion that these cortical areas are the sources of the N1. On the other hand, these areas may be involved in the generation of the N1 if the temporo-parietal generators are dependent on integrative transcallosal communication (Knight et al., 1980). Intracranial recordings in human patients from the lateral cortical surface (Celesia et al., 1968, Celesia, 1976, Kropotov et al., 2000) and from the primary auditory cortex (Kropotov et al., 2000) detected responses to auditory stimulation in the time range of long latency scalp-recorded potentials. Intracranial recordings with depth electrodes (Ervin and Mark, 1964; Velasco et al., 1985; Velasco and Velasco, 1986) detected activity that correlated to the scalp-recorded N1 in several subcortical structures: medial and dorsal thalamus, striatum, limbic system, and reticular formation, while no long-latency responses were observed in specific sensory thalamic nuclei. At present, it is evident that the N1 wave originates from several anatomically and functionally distinct sources (Näätänen and Picton, 1987; Alcaini et al., 1994; Giard et al., 1994; Woods, 1995; Picton et al., 1999).

The developing of source modeling techniques allowed the localization of the predominant generators of both the magnetic (bilateral tangential) and electric N1 (bilateral radial and tangential) in the vicinity of the auditory cortex (Hari et al., 1982; Scherg and von Cramon, 1986). Furthermore, in accordance with the anatomical hemispheric asymmetry of the Heschl's gyrus and the planum temporale (Rojas et al., 1997, Westbury et al., 1999), the supratemporal source of the N1 in right-handed subjects is usually located more anteriorly in the right than the left hemisphere (Nakasato et al., 1995; Ohtomo et al., 1998; Pantev et al., 1998; Teale et al., 1998; Tiihonen et al., 1998; Tiitinen et al., 1999; Fujioka et al., 2002).

Employing brain electric source analysis technique, Giard et al. (1994) localized an additional frontal generator of the N1 on the medial surface of the frontal lobes, which could be activated by cortico-cortical connections from the temporal lobes (Pandya and Seltzer, 1982) and by direct projections from subcortical nuclei (Thompson and Masterton, 1978; Kulikov, 1994). The frontal source determined by Giard et al. (1994) was activated even at ISIs as short as one second. However, responses to the first stimulus of a train (after a 1-2-minute time interval) showed different current configurations, suggesting the involvement of different neural mechanisms in infrequent stimulation processing. This finding has been confirmed by Alcaini et al. (1994) and allowed to conclude that the frontal component elicited by frequent stimulation can be considered as obligatory (Giard et al., 1994). On the other hand, a frontal generator could serve stimulus detection by triggering attention to it.

Picton and colleagues (1999) using both discrete and distributed approaches identified 10 sources for the N1: two bilateral regional sources composed of three orthogonal dipoles were located in the supratemporal plane, two sources in the posterior regions of the frontal lobes, suggesting some activity in the cingulate cortex or supplementary motor areas, and two sources in the frontal pole regions. Distributed inverse solution employed in the same study did not isolate frontal activity since it was relatively weak compared to the concomitant activity in the temporal lobes. In the study by Lavikainen et al. (1994), an additional parietal source was suggested to contribute to the generation of the N1m and P2m components.

The location of the tangential supratemporal generator of the N1 was shown to be dependent on the tonal frequency (Elberling et al., 1982; Hari and Mäkelä, 1986; Yamamoto et al., 1992; Pantev et al., 1995; Rosburg et al., 2000). Results from several studies suggest that higher frequencies activate more medial regions of the auditory cortex than lower frequencies (Yamamoto et al., 1992; Tecchio et al., 2000; Rojas et al., 2002). Furthermore, in some of these studies the depth of the dipole increased linearly with the logarithm of the stimulus frequency (Tecchio et al., 2000; Rojas et al., 2002). This finding was usually interpreted as a reflection of tonotopic organization of the auditory cortex. Studying both middle and long latency responses, Pantev and colleagues (1995) showed that the positions of the N1 and Pa generators varied as a function of frequency in opposite directions: in contrast to the N1, the sources of the Pa were located more laterally with increasing stimulus frequency, suggesting at least two tonotopically organized areas. On the other hand, a detailed comparison of the results from different studies revealed major discrepancies (Lütkenhöner et al., 2003). In some studies only the dipole's orientation but not spatial location correlated with the sound frequency (Tiitinen et al., 1993; Verkind et al., 1995; May et al., 1999). In other studies neither location nor orientation of the N1 source was dependent on the frequency of the sound (Stufflebeam et al., 1998; Hirata et al., 1999; Fujioka et al., 2002). Even if a clear frequency dependence was found, the locations of the N1 generators activated by high and low frequencies could differ in all possible directions: in medio-lateral, as mentioned above, in antero-posterior, with the N1 source for high compared to low frequencies located either more posteriorly (Elberling et al., 1982; Rosburg et al., 2000) or more anteriorly (Hari and Mäkelä, 1986), and in infero-superior direction (Rosburg et al., 1998). There is accumulating evidence indicating that the human auditory cortex consists of multiple tonotopically organized areas, and all these areas are highly interconnected. At the time range of the N1 all of them are probably simultaneously active. As a consequence, various areas each with a separate tonotopic organization contribute with different weightings to the resulting magnetic field (Hari, 1990; Lütkenhöner et al., 2003). This seems to be a logical explanation for the considerable discrepancy among the studies.

The location of the generator of the N1m was also shown to be dependent on the stimulus intensity (Pantev et al., 1989; Mäkelä and Hari, 1990), providing evidence for an amplitude organization of the auditory cortex. However, taking into account the complex functional anatomy of the supratemporal cortex, we face the same problem that was discussed regarding tonotopy. Nevertheless, it seems plausible that the location of the N1 source is a function of two independent variables – the frequency and intensity of the stimulus (Näätänen, 1992).

The spatial location of the sound has also been shown to affect the N1 response. Its amplitude was enhanced when stimuli were presented alternatively from different loudspeakers than from the same one (Butler, 1972). Furthermore, this effect was stronger when the loudspeakers were separated in the horizontal than vertical plane. There is also some evidence that interaural time and intensity differences at the time range of the N1 may be processed in different areas in the auditory cortex (Ungan et al., 2001), indicating that convergence of these two localization cues takes place at a hierarchically higher level.

2.3.2. P2

In the earlier studies, the N1 and P2 waves were traditionally analyzed as a complex because it had been noticed that the P2 covaried with the N1 along different stimuli dimensions. However, now it is clear that these two peaks “do not represent a single cerebral event” (Näätänen, 1992). Typically, the N1 and P2 have different scalp topography with the amplitude maximum shifted slightly posteriorly for the P2 (Roth et al., 1976; Hari et al., 1982; Paavilainen et al., 1991). In the study by Roth et al. (1976) the P2 was shown to be more strongly affected by the ISI than the N1, although both peaks were attenuated by shortening ISIs. Unilateral temporal lesions reduce both the N1 and P2 contralaterally to the damaged hemisphere (e.g., Peronnet et al., 1974). Results from a study by Knight et al. (1980) demonstrated that, in contrast to the N1, neither frontal nor temporo-parietal lesions produced a significant effect on the P2, suggesting that these two responses originate from distinct neuronal sources.

There is not much data concerning the generators of the P2. The predominant generators of the P2 are also located bilaterally on the superior surface of the temporal lobes, with the right-hemispheric generator being located more anteriorly than the left-hemispheric homologous. They were shown to be located more anteriorly in respect to the N1 sources in both hemispheres (Hari et al., 1987; Tiitinen et al., 1999). Although the location of the P2 sources is usually independent of the frequency and intensity of the sound, the P2 may also have specific and nonspecific components (Näätänen, 1992). For instance, the P2 may partially reflect the auditory driven output of the mesencephalic reticular activating system (Knight et al., 1980; Rif et al., 1991). In the study by Anderer et al. (2004) employing low-resolution brain electromagnetic tomography for the analysis of the electric sources of auditory ERPs, the bilateral activations in the superior temporal gyri in the time-range of the P2 component were accompanied by a medial activation of the precuneus.

2.3.3. N2

The N2 is traditionally thought to be an endogenous component since it is usually elicited by unexpected infrequent stimuli (Duncan-Johnson and Donchin, 1982; Ahveninen et al., 2002), omitted stimuli (Simson et al., 1976), as well as in classification (Ritter et al., 1982 and 1983) and target-detection tasks (McCallum et al., 1989; Anderer et al., 2004). This deflection is usually followed by the P3 component and is associated with control rather than automatic processes (Näätänen and Picton, 1986). The endogenous N2 to auditory stimuli has typically a frontal or central scalp distribution (Näätänen and Gaillard, 1983; Enoki et al., 1993), and this distribution is modality specific (Simson et al., 1977). Importantly, besides specificity to the modality, the scalp distribution of the N2 may also depend on the stimulus class within the same modality (Ritter et al., 1983). Furthermore, its amplitude may be modulated by alterations in a certain stimulus attribute in the divided attention task (Omoto et al., 2001), suggesting that the N2 component may be related to stimulus classification.

The data about the generators of the N2 wave are relatively scarce. This peak was suggested to be generated in the vicinity of the supratemporal planes, possibly including frontal activity (Ceponiene et al., 2002). Data from the study by Anderer and colleagues (2004) suggest superior temporal gyrus, precuneus, and medial anterior cingulate structures as possible cortical generators of the N2 component.

The amplitude and latency of the N2 were shown to vary as a function of the difficulty of discrimination (Fitzgerald and Picton, 1983; Näätänen and Picton, 1986). The N2 amplitude is larger and the latency longer when the target is more difficult to discriminate. Consequently, the N2 may be related to the effort required to discriminate the target stimuli (Fitzgerald and Picton, 1983; Näätänen and Picton, 1986). The latency of the N2 was also shown to increase with memory load (Wolach and Pratt, 2001). In another working memory study employing Sternberg's paradigm, the latency of the N2 was prolonged by distracters qualitatively similar to the memorandum (spoken digits) as compared with other type of interfering stimuli (noise bursts) (Wolach and Pratt, 2001).

Interesting results were obtained from the analysis of the error responses in the study by Leppert and colleagues (2003). When the subjects were aware that they had made an error, endogenous components (both N2 and P3) were delayed and attenuated, whereas when the subjects were unaware of the error, no endogenous ERP could be identified. This finding supports the view that endogenous components depend upon stimulus recognition, since when the target was not recognized and the error not noticed, the brain events were associated with the processing appropriate to the frequent non-target stimulus.

Since the N2 has been shown to correlate with reaction times, it has been proposed to reflect a target selection and decision process that controls behavioral responses in sensory discrimination tasks (Ritter et al., 1979). Furthermore, the N2 was also observed in responses to targets when a delayed response or no motor response (but silent counting of targets) was required and thus it was uncontaminated by activity related to the organization of movement, representing "pure" indices of the discriminative process (Simson et al., 1977). In a later study, however, Ritter et al. (1983) refused the view that the N2 would reflect target selection, because its latency in a simple reaction time task was too long with regard to reaction times.

The finding that the N2 was enhanced in no-go trials led to the conclusion that this peak might reflect response inhibition processes (Pfefferbaum et al., 1985; Eimer, 1993; Kopp et al., 1996; Falkenstein et al., 1995 and 1999). The "no-go N2" was observed in both motor and covert response trials when the subjects had to imagine but not perform the button pressing (Burle et al., 2004).

Several observations indicate that the N2 component (so-called "basic" N2) may also be elicited automatically and therefore fulfills the criteria of obligatory components. It may be observed even in the responses to repetitive homogenous stimuli (Näätänen and Picton, 1986). The "basic" N2, clearly observed in children, however, is not always seen in adults. Results from several comparative studies indicate that during the course of maturation the amplitude of the N2 gradually decreases and its latency prolongs (Enoki et al., 1993; Karhu et al., 1997; Ponton et al., 2000 and 2002). The N2 is typically observed in responses to both target and

non-target deviants in the attended input (Näätänen et al., 1982; Alho et al., 1990), although wide deviations in the unattended input may also elicit the N2 (Näätänen et al., 1982), which was suggested to reflect transient arousal or orienting response (Näätänen and Gaillard, 1983; Loveless, 1986; Näätänen, 1992). Paavilainen and colleagues (1991) have demonstrated the N2 component in the responses to some classes of deviants (namely duration and intensity) in the ignore condition. The N2 may be also elicited by variable equiprobable stimuli in both attended and passive listening conditions. In the detection condition, however, the N2 is enhanced for both targets and non-targets in the attended input (McCallum et al., 1989).

In conclusion, the N2 elicited by task-irrelevant stimulus changes (e. g., in unattended input, in ignore condition or in simple reaction task compared to active discrimination) may be related to automatic processes, whereas the N2 elicited during discrimination and classification tasks may be associated with control processes (Ritter et al., 1983; Näätänen and Picton, 1986).

2.3.4. P3 and Positive Slow Wave (PSW)

Since its description by Sutton and colleagues in 1965, the P3 has become one of the most extensively studied components of the human evoked response. Typically elicited in the oddball paradigm, the P3 is known as the prominent positive peak of event-related potentials with an amplitude maximum over the centro-parietal area of the scalp and a latency of 300–500 ms (Smith et al., 1970; Fabiani et al., 1987). The P3 has been suggested to reflect a number of cognitive processes related to the detection of a target or an omitted stimulus (Sutton et al., 1967; Picton and Hillyard, 1974), such as the assessment of stimulus relevance, decision making, control of updating process, and perceptual closure at the completion of processing (Desmedt, 1980; Picton, 1992; Andreassi, 1995). It has also been linked to the updating of a cognitive model of the environment within working memory stores (Donchin and Coles, 1988). The statement that the P3 may reflect decision making seems, however, questionable, because reaction times in relatively simple tasks are often shorter than the peak latency of the P3. Thus the P3 rather indexes the percepto-motor sequel of the decision (Picton and Hillyard, 1974). The P3 may be elicited even in the passive listening condition when multiple equiprobable stimuli are employed (McCallum et al., 1989). However, in the target detection condition (when a motor response to one of these equiprobable stimuli is required), the amplitude of the P3 is significantly increased in the responses to both targets and non-targets.

The P3 elicited in passive oddball tasks to unpredicted novel and highly deviant events is referred to as P3a and thought to indicate involuntary capture of attention or orienting, which make events available to conscious evaluation and behavioral control (Squires et al., 1975; Friedman et al., 2001). Differing from the P3b elicited by targets in active tasks, the P3a has a shorter latency and more frontal scalp distribution, and, similarly to the P3b, it is also influenced by stimulus probability. Both the P3a and P3b are larger in responses to less frequent events (Duncan-Johnson and Donchin, 1977; Friedman and Simpson, 1994). Another specific feature of the P3a is that it habituates very rapidly with a stronger amplitude decrease over frontal than parietal sites (Friedman and Simpson, 1994). The P3a may also be elicited by targets in active oddball tasks thus reflecting any changes in the ongoing sequence of events

regardless of whether they are attended or not (Squires et al., 1975). Thus, the P3a and P3b may co-occur within the same waveform in responses to targets (Squires et al., 1975; Friedman et al., 2001). Since the present review will address exclusively the slow responses elicited in active tasks, the positive deflection with the latency around 300 – 400 ms will be referred to as the “P3”.

The P3 has been shown to be affected by a variety of factors, both internal (e.g., arousal, emotion, fatigue, and age) and external (e.g., drugs) (Polich and Kok, 1995). It has been shown to decline in the course of long-term habituation (Woods and Elmasian, 1986). In contrast to the N1, the P3 demonstrated stimulus non-specific long-term habituation. The effect of memory load on the amplitude of the P3 component has earlier been shown in different studies employing either the n-back task (McEvoy et al., 1998) or Sternberg’s paradigm (Pratt et al., 1989a; Pratt et al., 1989b; Pelosi et al., 1998; Grippo et al., 1996). In most studies, the amplitude of the P3 was reported to be higher in the low load than the high load task. This relationship between the amplitude of the P3 component and memory load has been observed for probe stimuli (Pratt et al., 1989a; Pratt et al., 1989b; Pelosi et al., 1998, Grippo et al., 1996) and memory set items (Pratt et al., 1989c). The decrease of the P3 amplitude with increasing memory load has been associated with the reduced capacity of attention directed to the single item during working memory processing (Wickens et al., 1982). However, when the ERPs were compared in relation to the serial position of the memory cue (Pratt et al., 1989c), a significant increase was found in the P3 amplitude from the first to the middle and last items.

In paradigms with complex tasks that involve either perceptual difficulty (Ruchkin et al., 1988) or a high working memory load (Garcia-Larrea and Cezanne-Bert, 1998), the P3 component is often followed by a positive slow wave (PSW) (Squires et al., 1975). This deflection may be observed even in single trials (Loveless et al., 1987). The P3 and PSW can be dissociated on the basis of their distinct relationships to experimental manipulations (Ruchkin et al., 1990) such as variations of perceptual and conceptual difficulty, emotional content of visual stimuli or memory load. In the study by Ruchkin et al. (1988), the P3 was related to the conceptual difficulty while the PSW increased with perceptual difficulty. The amplitude of the P3 component described by Garcia-Larrea and Cezanne-Bert (1998), conversely, decreased with increasing subjective difficulty while the PSW was shown to increase in amplitude with the memory load. The authors suggested the PSW to reflect the retrieval of information from working memory. Similarly in the study by Pelosi et al. (1992) employing Sternberg’s paradigm, the amplitude of the earlier positive peak (P400) decreased significantly with increasing memory set size, but the amplitude of the next positive component (P560) was either preserved or even enhanced.

The amplitude of the P3 component has also been shown to be sensitive to the emotional content of visual stimuli in both early (300-400 ms) and late (380-440) time windows (Keil et al., 2002). In the early time window, the global field power was enhanced by both pleasant and unpleasant pictures compared to neutral pictures; in the late time window the global field power enhancement was due specifically to the processing of unpleasant pictures.

The processing of error responses in the discrimination task revealed that in the error compared to correct trials the amplitude in the P3 range was reduced, while the positive slow wave was enhanced (Falkenstein et al., 1991). Since the difference in the ERP magnitude between correct and incorrect responses reached maximum over the fronto-central rather than parietal sites the authors suggested that it was due not to the P3 modulation but to an additional process, "error negativity", occurring in error trials. The "error negativity" was time-locked more closely to the motor response than to the stimulus and was proposed to reflect an automatic mismatch between the overt response and outcome of the response selection process. The positive slow wave, in turn, was proposed to reflect the conscious evaluation of the error. Other evidence for the dissociation of the P3 and PSW came from their different correlations with reaction times (RTs) (Ruchkin et al., 1980). In the study by Roth et al. (1978), the amplitude of the P3 decreased and the PSW increased with the increase of the RTs. Similar tendency was described in the paper by Pelosi et al. (1992): the P560 wave was observed more frequently in trials with "slow" behavioral responses while P400 was significantly reduced in trials with "slow" compared to "fast" responses. However, the P3 and PSW are not always easily dissociable and are therefore analyzed as a single peak, which may obscure possible amplitude or latency differences between experimental conditions.

Despite the various methodologies employed, the locations of generators of these slow endogenous responses are not unequivocally known. Different source localization techniques, event-related fMRI and intracranial recordings have suggested several cortical regions and deep subcortical structures as possible generators of the P3 component. The reports of studies employing intracranial recordings commonly agree that medial temporal lobe structures, including the hippocampus and parahippocampal gyrus, have a role in target detection (McCarthy et al., 1989; Smith et al., 1990; Paller et al., 1992; Halgren et al., 1995a,b; Kanovsky et al., 2003). Polarity reversals along the surface of the medial temporal lobe may indicate local sources of recorded P3-like potentials, however, these potentials were delayed by 50 ms compared to scalp-recorded P3 (Halgren et al., 1995b, 1998). Although some clinical observations have indicated local attenuation of the P3 after temporal lobectomy (Daruna et al., 1989), generally, results from lesion studies are highly inconsistent (Moores et al., 2003). Therefore, it is not clear whether medial temporal lobe structures have an essential contribution to the scalp-recorded P3 (Moores et al., 2003). Intracranial recordings have also revealed P3 generators within the inferior parietal lobuli (Smith et al., 1990), the superior temporal sulcus (Halgren et al., 1995b, 1998) and parieto-occipital region (Kiss et al., 1989). Event-related fMRI has allowed the detection of a number of cortical regions specifically activated during target processing, including the supramarginal gyrus, middle frontal gyrus, frontal operculum, anterior cingulate, middle and superior temporal gyri, inferior and superior parietal lobules, and the precuneus (McCarthy et al., 1997; Menon et al., 1997; Linden et al., 1999; Kirino et al., 2000; Kiehl et al., 2001; Horowitz et al., 2002; Horn et al., 2003).

Recent combined electrophysiological and neuroimaging studies have enabled the analysis of correlations between the amplitudes of evoked responses and regional hemodynamic responses. Activation in the supramarginal gyri, right medial frontal gyrus,

insula, and thalamus correlated with the P3 amplitude as a function of target probability in a combined EEG – fMRI study (Horovitz et al., 2002), suggesting that these regions are probable sources of the P3. In a combined EEG – PET study (Perrin et al., 2005), regional blood flow in the posterior part of the right superior temporal sulcus, the precuneus, and medial prefrontal cortex correlated with the amplitude of the P3 elicited by the subject's own name.

The development of source localization techniques such as equivalent current dipole-fitting and minimum-norm estimates has provided the possibility to determine the generators of the components of evoked responses obtained in multichannel EEG and MEG recordings. In the studies employing the dipole-fitting algorithms, both cortical (mainly in the temporal lobes) and deep subcortical (thalamus) structures were often suggested to generate the P3 in target recognition tasks (Rogers et al., 1991; Mecklinger et al., 1998; Tarkka et al., 1995; Hegerl and Frodl-Bauch, 1997; Frodl-Bauch et al., 1999). However, referring to the results from simulation studies (George et al., 1995), it has been pointed out that the use of dipole-fitting algorithms might result in errors concerning the depth of broad and extended sources (Moores et al., 2003). Another limitation of dipole modelling is the requirement of a priori assumptions of the number and possible locations of the estimated sources (Tarkka et al., 1995; Moores et al., 2003). Employing the cortical current density estimation allowed to identify both modality-specific and non-specific sources of the P3 in the visuo-verbal oddball study (Moores et al., 2003). Modality-specific sources were located in the lingual/inferior occipital gyrus and mid-fusiform gyrus, while intraparietal sulcus and surrounding superior parietal lobes were attributed to the working memory and attention processes and visuo-motor integration. Thus, algorithms that do not require any a priori knowledge about the number of the active sources or their spatial locations seem to be suitable tools for the analysis of the slow components of evoked responses.

To summarize, long-latency responses appear to be generated by distributed networks. Furthermore, while the N1 and, perhaps, the P2 have predominant sources in modality-specific areas, the later responses may reflect activity of a widespread associative cortical network.

3. THE AIMS OF THE PRESENT PROJECT

The purpose of this project was to study, employing different working memory paradigms, whether mnemonic processing of auditory spatial and nonspatial information is segregated in the human brain. Electrophysiological research techniques with excellent time resolution, which are able to detect even brief transient task-related differences between evoked responses, were used to investigate the timing of segregation. In addition, the MEG technique has a relatively good localization ability, which enables determination of cortical structures sensitive to sound attribute.

The main aims and questions addressed in the Ph.D. work are the following:

I. In the first study the aim was to test at the behavioral level whether a task-irrelevant selective interference affects differentially spatial and nonspatial auditory working memory task performances.

II. The aim of the second study was to test whether there is a difference in the distribution of slow memory-related potentials (late slow waves) during the retention of audiospatial and pitch information.

III. The third study was designed to test whether working memory processing of spatial and nonspatial auditory information affects transient components of auditory evoked potentials.

IV. The fourth study was conducted in order to test whether the increase of memory load differentially affects auditory evoked responses to memory cues recorded during location and pitch working memory task performance.

V. The aim of the fifth study was to investigate cortical generators of the slow components, the P3 and positive slow wave (PSW), of auditory evoked responses to probe stimuli recorded during spatial and nonspatial working memory tasks.

4. METHODS

In the following text the five studies will be referred to with corresponding Roman numerals I – V.

4.1. Subjects

Altogether 53 healthy right-handed volunteers with no history of hearing disorders participated in the experiments:

Study I. Twelve (6 females and 6 males, ages 17–29 years, mean 23 years)

Study II. Eleven (6 females and 5 males, ages 20-35, mean 24 years)

Study III. Eleven (5 females and 6 males, aged 19 – 30 years, mean age 25 years)

Studies IV-V. Nineteen (9 females and 10 males, aged 21 – 32 years, mean age 27 years).

Subjects gave an informed consent for participation in the studies, which were approved by the Ethical Committee of the Helsinki University Central Hospital.

4.2. Stimuli

Study I. In the first study the stimuli were three sinusoidal tones (1000, 2250 and 3375 Hz, duration 100 ms, rise/fall time 10 ms) delivered binaurally through earphones mimicking three presentation locations (left, middle, and right). The left and right locations were simulated by an interaural intensity difference of 17 dB (about 58 and 75 dB SPL for each ear, and the middle location by presenting the tones binaurally at an equal intensity of about 70 dB SPL. The interval between task-relevant stimuli was 3125 ms. In both the location and pitch tasks the stimuli were the same (the three locations and pitches of tones occurred equiprobably in a pseudorandom order), the type of task was specified by the instruction to attend either to the sound frequency or its spatial location, irrespective of another attribute.

The distracters were irrelevant to the n-back task performance and the subjects were instructed to ignore them. They were a pair of sinusoidal tones having equal parameters to the task-relevant stimuli (memoranda), presented in the middle of the delay between consecutive memoranda with the interval of 150 ms between distracters. The location distracters consisted of two tones of the same frequency (1000 Hz) occurring in two of the three different locations (left, middle and right). The pitch distracters consisted of a pair of tones having two of the three different frequencies (1000, 2250 and 3375 Hz) and presented in the middle location. The presentation of the stimuli was controlled by a computer program (Neurosoft, Inc.).

Study II. In the pitch task, the stimuli were sinusoidal tones (duration 100 ms, rise/fall time 10 ms) with three different pitches (equiprobably either 1000, 2250, or 3375 Hz) presented binaurally with an equal intensity (intensity about 70 dB SPL) through headphones with an interval of 3000 ms (delay period). In the location task, the stimuli were sinusoidal tones (duration 100 ms, frequency 2250 Hz) presented binaurally. Left and right locations were

simulated by an interaural intensity difference (about 17 dB SPL) and the middle location by presenting the tones binaurally with an equal intensity (about 70 dB SPL). The presentation of the stimuli was controlled by a computer program (Neurosoft, Inc.), which also collected behavioral data (correct and incorrect responses, misses, and reaction times).

Study III. Sinusoidal tones with duration of 100 ms including 10-ms rise and fall times and frequency of 1000 or 1500 Hz were presented binaurally through plastic tubes and earpieces. Left (L) and right (R) locations were simulated by an interaural intensity difference. The intensity in the ipsilateral channel was 75 dB SPL and the opposite channel was attenuated by 17 dB. In both the location and pitch tasks the stimuli were identical (the two locations and frequencies of tones occurred equiprobably in a pseudorandom order), the type of task was specified by the instruction to attend either to the sound frequency or its spatial location, irrespective of another attribute. The presentation of the stimuli was controlled by a computer program (Neurosoft, Inc.), which also collected behavioral data (correct and incorrect responses, misses, and reaction times).

Studies IV-V. The stimuli were sinusoidal tones (duration 200 ms, including 10-ms rise and fall times) with a frequency of 220, 440 or 880 Hz. They were presented binaurally through plastic tubes and earpieces. Left (L) and right (R) locations were simulated by both an interaural intensity difference of 13 dB and an interaural time difference of 500 μ s. For the L and R sounds, the intensity in the ipsilateral side was 75 dB SPL and was attenuated in the contralateral side. The middle (M) location was simulated by binaural presentation of symmetrical tones. For the M sound, the intensity in both channels was attenuated by 5 dB. Furthermore, the subjective loudness of the sounds was adjusted by attenuating the intensity bilaterally by 3 dB for the sounds with the frequency of 440 Hz and by 6 dB for 880 Hz. Similar blocks of stimuli were used in both the location and pitch tasks: 3 frequencies and 3 locations were mixed in a pseudorandom order, providing 9 possible combinations of stimulus attributes. The tasks differed from each other only with respect to the instruction to attend either to the sound frequency or its spatial location, irrespective of another attribute. The delivery of the stimuli was controlled by a computer program (Presentation 0.31, Neurobehavioral Systems, Inc., San Francisco, USA), which also collected the behavioral data (correct and incorrect responses, and reaction times).

4.3. Tasks

The hypothesis of the dissociation between spatial and nonspatial auditory information processing was tested using several working memory paradigms.

Study I. In the first study location and pitch *n-back tasks* with two load levels (1-back and 2-back) were used. Task-irrelevant auditory distraction was presented in part of the experimental blocks in the middle of the delay (Fig. 4.3.1). In the 1-back tasks, the subjects were instructed to compare each task-relevant stimulus in the sequence with the previous one and to press the left

button with the index finger whenever the tone had the same frequency (pitch task) or occurred in the same location (location task) as the previous one (match trials, 33%). If the sounds did not match in respect to attended attribute, the subjects were to press the right button with the middle finger (non-match trials). In the 2-back tasks, subjects had to compare each stimulus in the sequence with the stimulus presented two trials back.

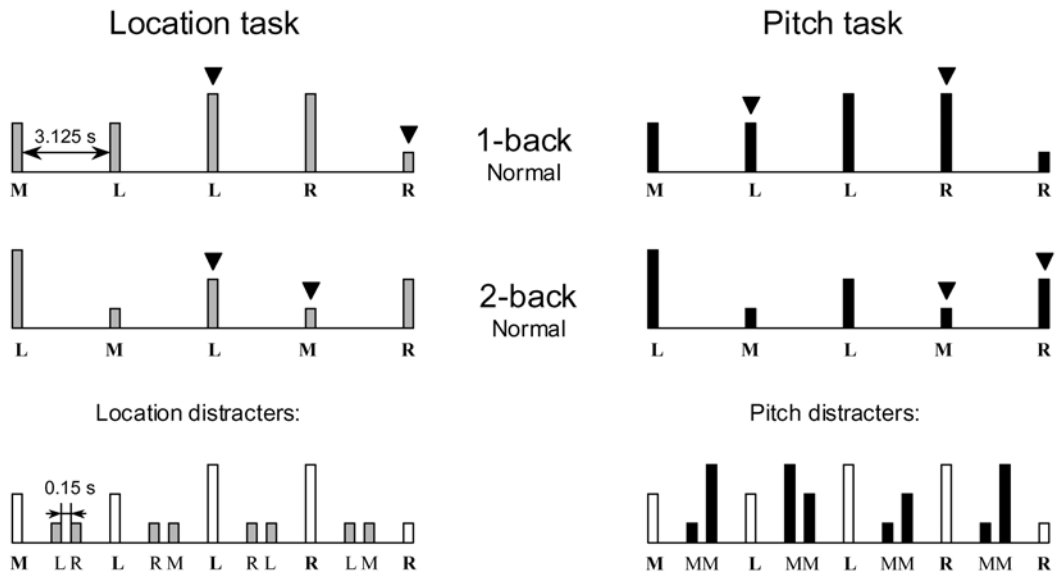


Fig. 4.3.1. Illustration of the 1- and 2-back location and pitch tasks. The height of the bar represents the pitch of the tone (1000, 2250 or 3375 Hz). L = left, M = middle and R = right presentation locations. Triangles indicate match trials and arrows the time intervals in seconds.

Study II. In the second study location and pitch *n-back tasks* with two load levels (1-back and 3-back) were employed (Fig. 4.3.2). In the 1-back task, the subject pressed the left button whenever the stimulus occurred in the same location (location task) or had the same pitch (pitch task) as the previous stimulus, and in the 3-back task whenever it was in the same location or had the same pitch as the stimulus presented three trials back (match trials, 33%). In non-match condition the subject was instructed to press the right button.

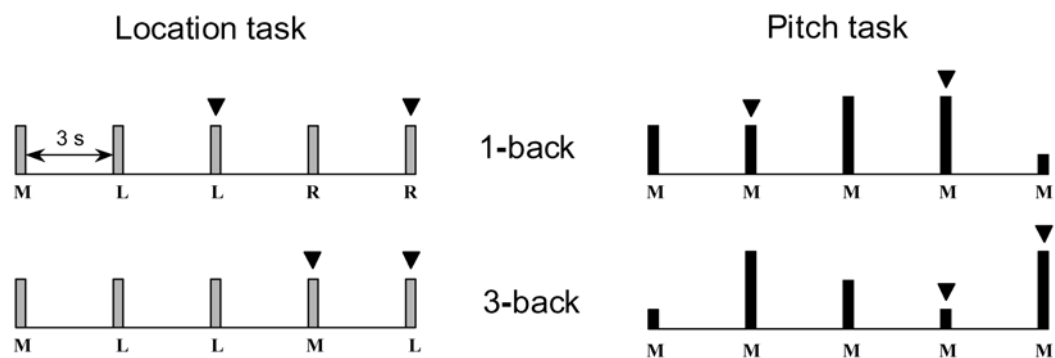


Fig. 4.3.2. Illustration of the 1- and 3-back location and pitch tasks. All explanations as in Fig. 4.3.1.

Study III. Location and pitch *delayed matching-to-sample tasks* were used in the third study. The trials started when a fixation cross appeared on a screen (Fig. 4.3.3). After a fixation time of 1 s, a cue with a frequency of 1000 or 1500 Hz was presented in one of the two locations (L or R). At the end of the delay period of 1.9 s, a probe stimulus was presented which was equiprobably either 1000 Hz L, 1000 Hz R, 1500 Hz L or 1500 Hz R. The subjects were instructed to press the left button of a response pad with the right index finger if the stimulus was of the same frequency as the cue in the pitch task or in the same location as the cue in the location task (match condition). In the non-match condition the subjects were instructed to press the right button with the right middle finger. Match and non-match trials were presented with an equal probability in a random order. The subjects were instructed to respond as fast and as accurately as possible and to continue visual fixation until the fixation cross was turned off 2 s after the onset of the second stimulus. The intertrial interval (rest) was of 2 s.

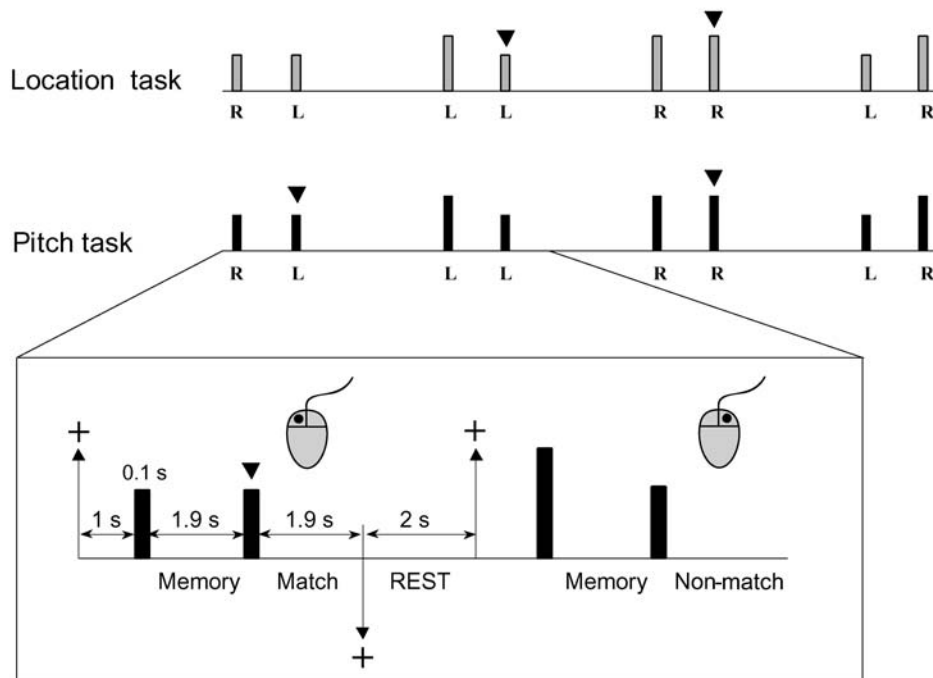


Fig. 4.3.3. Illustrations of the behavioral tasks and experimental design. The height of the bar represents the frequency of the tone (1000 or 1500 Hz). + = fixation cross, vertical arrows indicate time points when the fixation cross turns on (up) and off (down). Motor response (button pressing) is symbolized with a computer mouse. All other explanations as in Fig. 4.3.1.

Studies IV-V. For the fourth and fifth studies a *new behavioral paradigm* was designed, which combines features of the n-back and delayed matching-to-sample tasks (Fig. 4.3.4). One trial consists of 6 stimuli: the first three are memory cues, and the last three are probes. Subjects had to compare the first stimulus with the 4th, the second with the 5th and the third with the last one, and to decide whether it was the same or different in respect to attended sound attribute. As an n-back task, this design enables variation of the memory load in a parametric manner; as a matching to sample task – separation of “cue” and “probe” conditions, providing recording of memory-related responses that are not biased by a motor-

related activity, and, differing from Sternberg's paradigm, it enables a high behavioral control of task performance. The trials started when a fixation cross appeared on the screen. After a fixation time of 1 s, the first cue was presented. The time between the onsets of successive stimuli within one trial was 2 sec. Motor responses were required only for the probes. The subjects were instructed to press the left button of a response pad if the probe stimulus was of the same frequency as the cue in the pitch task or in the same location as the cue in the location task (match condition). In the non-match condition, the subjects were instructed to press the right button. Matching and non-matching probes were presented with an equal probability in a random order. The subjects were instructed to respond as fast and as accurately as possible and to continue visual fixation until the fixation cross was turned off 2 s after the onset of the last stimulus of the trial. The intertrial interval (rest) lasted 2 s.

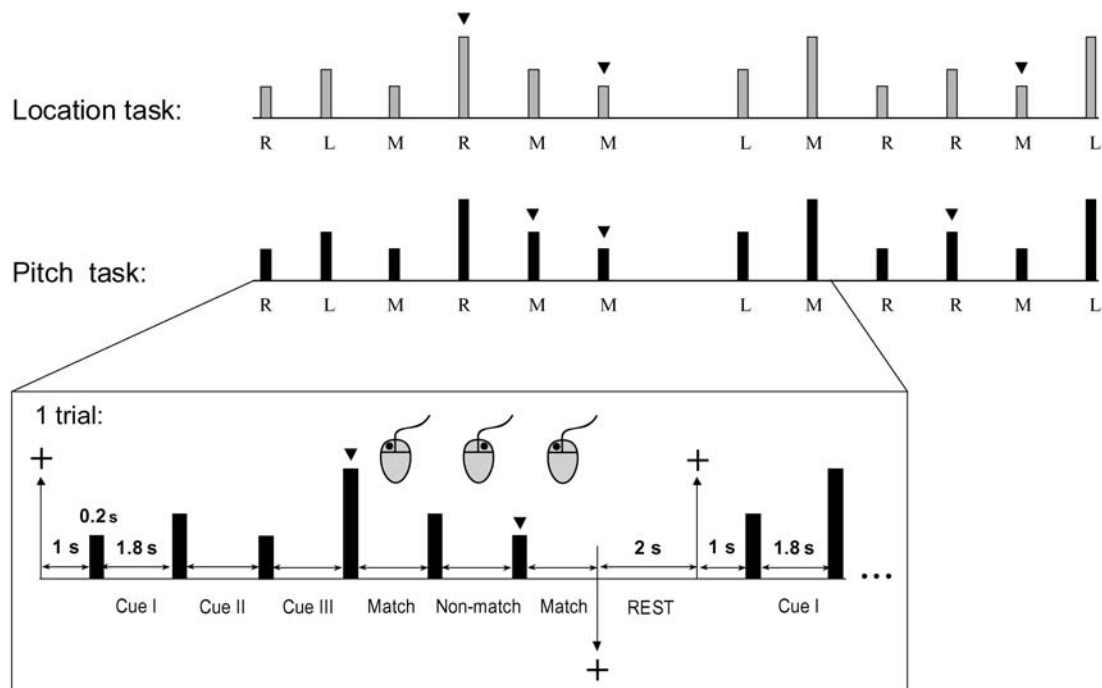


Fig. 4.3.4. Illustrations of the behavioral tasks and experimental design. The height of the bar represents the frequency of the tone (220, 440 or 880 Hz). All other explanations as in Fig. 4.3.1. and 4.3.3.

4.4. Data collection and analysis

Study I. The behavioral data (correct and incorrect responses including false alarms and misses, and reaction times) were collected by Neuroscan hardware and Respwin software. Two-way analysis of variance for repeated measures (2-ANOVAs, BMDP program package) was used to test the main effects of Task (location vs. pitch), Load and Condition (normal, location and pitch distraction) on the number of incorrect responses, reaction times of correct responses and subjective difficulty level. If the ANOVA gave a significant main effect ($p < 0.05$), the further analyses were performed using Wilcoxon nonparametric (accuracy data, difficulty level) or Student's parametric t-tests (reaction time data).

Study II. Electroencephalogram (EEG) was recorded with Ag-AgCl cup electrodes according to the international 10-20 system from 21 positions on the scalp. In all electrophysiological studies (II-V) the reference electrode was placed on the nose and the ground electrode on the left cheek; in addition, vertical and horizontal electrooculograms (EOG) were recorded. In study II, electrical activity was amplified (1000 x) with DC amplifiers, low pass filtered at 100 Hz, and digitised with Neuro Scan system (sampling frequency 500 Hz). ERPs were obtained by averaging EEG epochs recorded over a period of 3000 ms starting 200 ms before each stimulus. EEG epochs containing errors and excessive eye-movements or blinks were discarded from the averaging. The magnitude of the slow potentials during the delay period was measured as the mean amplitude over three fixed time windows: 700-1400 ms (early phase), 1400-2100 ms (middle phase), and 2100-2800 ms (late phase) after stimulus onset. Analyses of variance for repeated measures (ANOVAs, BMDP program package) were used to test the main effects of Task, Load, and Electrode Matrix (frontal vs. parieto-occipital) on slow potentials. The behavioral data were analyzed using 2-way ANOVA with factors been Task and Load.

Study III. The magnetoencephalogram (MEG) was recorded in a magnetically shielded room with a 122-channel whole-head magnetometer (Neuromag Ltd., Helsinki). The electroencephalogram (EEG) was simultaneously recorded with a 64 Ag/AgCl-electrode cap. The analog recording passband was 0.03–100 Hz, the sampling rate was 300 Hz. Epochs containing artifacts or incorrect responses were automatically rejected from the analysis. For both location and pitch tasks, three different conditions were analyzed: memory, match and non-match. The averaged responses (epoch from 200 ms before to 1500 ms after the cue) were digitally filtered with a passband of 1–30 Hz.

The amplitudes of the electrical ERP components were determined within sets of nine electrodes chosen according to the spatial distribution of each component (Fig. 5.5, A). A fronto-central set was used for the N1 component, a central set for P2, a frontal set for N2, and a parietal set for P3. The amplitudes of the ERP components were determined at the latency of the peak amplitude of the representative electrode site (at the center of the set) individually for each subject from each electrode site of the given set. The N1 component was determined as the most negative peak within the 80–130-ms time window, P2 as the most positive peak within the 140–260-ms window, N2 as the most negative deflection following P2 within the 170–350-ms window, and P3 as the most prominent positive peak within the 250–450-ms window. Peak latencies of the N1 component, which was the focus of interest in this study, were analyzed for each electrode site included in the fronto-central set. Statistical analysis of the peak latencies of other ERP components was performed for the representative electrode sites.

MEG dipole modeling was performed with Neuromag software using a standard spherical head model (origin at $x = 0$, $y = 0$, $z = 45$ mm). The coordinates of N1m sources were determined within a 70–120-ms time window using a 2-dipole model (one dipole for each

hemisphere). Peak latencies and equivalent current dipole (ECD) amplitudes as well as the goodness of fit were determined from the time-course curves of the sources.

For all statistical comparisons of the MEG and EEG data, a 3-way analysis of variance (ANOVA) for repeated measures was applied, with the factors being Task, Condition and Electrode (for the electric N1, 9 sites) or Hemisphere (for the N1m, left vs. right). Post hoc analyses were performed using the Newman–Keuls test. Statistical analysis of the behavioral data was performed using the paired nonparametric Wilcoxon’s signed-ranks test (accuracy and subjective difficulty level) and the paired parametric t-test (reaction times). The Greenhouse–Geisser correction was always used for factors with more than two levels.

Studies IV-V. The magnetoencephalogram (MEG) was recorded in a magnetically shielded room with a 306-channel whole-head magnetometer VectorView (Neuromag OY, Finland). The electroencephalogram (EEG) was simultaneously recorded with a 60-channel Ag/AgCl-electrode cap. The analog recording passband was 0.03–100 Hz and the sampling rate 600 Hz. Epochs starting 100 ms before and ending 1500 ms after the auditory stimulus onset were averaged online. The epochs containing artifacts or incorrect responses were automatically rejected from the analysis. In Study IV, in order to estimate task-related differences as a function of memory load, ERPs to the memory cues in the three consecutive epochs were analyzed for both location and pitch tasks: cue I (corresponding to the processing of one item in working memory), cue II (corresponding to the processing of two items), and cue III (processing of three items). In study V responses to probes were analyzed separately in match and non-match conditions for both location and pitch tasks.

Responses to memory cues (Study IV). The ERP components were analyzed after digital filtering with a passband of 0.5–20 Hz. Their amplitudes were determined within sets of nine electrodes (Fig. 4.4.1, A, B). A fronto-central electrode set was used for the N1 component, a central for P2, a frontal for N2, a centro-parietal for P3, and a parietal set for the positive slow wave (PSW). The amplitudes of the ERP components were determined as the mean amplitudes over a 30- (for the N1, P2 and N2) or 50-ms (for the P3) time window around the peak latency of the given component at the representative electrode site, individually for each subject from each electrode site of a given set. Statistical analysis of the peak latencies of all ERP components was performed for the representative electrode sites. The N1 component was determined as the most negative peak within the 70–120-ms time window, P2 as the most positive peak within the 140–260-ms window, N2 as the most negative deflection following the P2 within the 170–350-ms window, P3 as the most positive peak within the 230–450-ms window. The amplitude of the PSW was measured as the mean amplitude of the ERPs within the 450–650-ms window. Long-duration slow potentials, or late slow waves (LSW), were examined after low-pass filtering the averaged responses at 20 Hz. The magnitude of the slow waves during the three delay periods (cue I, II and III) was determined as the mean amplitude of the ERP over a time window of 500–1500 ms. This analysis was performed within arrays of 15 frontal and 14 parietal electrodes where the delay-related slow activity was most prominent (Fig. 4.4.1, C).

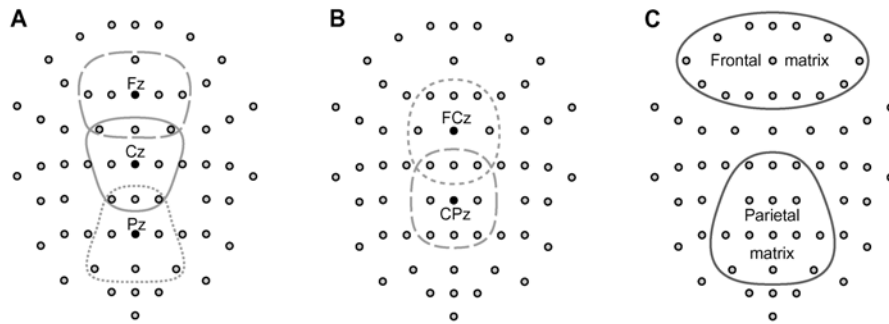


Fig. 4.4.1. Arrays of electrodes for the analysis of ERP components. (A) The 9-electrode sets: frontal (for N2), central (for P2) and parietal (for PSW). (B) Fronto-central (for N1) and centro-parietal (for P3) 9-electrode sets. Filled circles indicate representative sites. (C) The frontal and parietal matrices for the analysis of LSW.

MEG dipole modeling was performed with Neuromag software using a spherical head model. The origin of the spherical model was determined individually for each subject on the basis of his/her anatomical MRI by fitting a sphere to the curvature of the outer surface of the brain in temporal and centro-parietal cortical areas. Averaged MEG signals were digitally filtered with a passband of 1 – 30 Hz. The MEG data of two subjects were excluded from the analysis because of excessive noise in the recording. The coordinates of the N1m sources were determined within a 30-ms time window using a 2-dipole model. Peak latencies and ECD amplitudes were determined from the time-course curves of the sources. Anatomical MRIs with 1-mm isotropic voxels were acquired with a Siemens Vision 1.5-tesla system (Erlangen, Germany) using a T1-weighted three-dimensional MPRAGE sequence.

For statistical comparisons of the EEG and MEG data, a 2- or 3-way ANOVA was applied. The amplitudes and latencies of the transient ERP components were analyzed with the factors being Task, Condition (cue I - III) and Electrode (for the ERP amplitudes, 9 sites) or Hemisphere (for the N1m, left vs. right). The magnitudes of the LSW were analyzed with a 3-way ANOVA with the factors of Task, Condition and Electrode (14 or 15 sites). Post-hoc analyses were performed using the Newman–Keuls test.

Responses to probes (Study V). The amplitudes of the ERPs to probes were determined within a set of 15 electrodes centering on the parietal midline electrode (Pz) (Fig. 4.4.2). The amplitudes of the ERP components were determined as the mean amplitudes over a 50-ms time window around the peak latency at the Pz electrode site. Statistical analysis of the peak latencies of ERP components was performed for the Pz electrode site. The P3 component was determined as the most positive peak within the 250–450-ms time window, and the PSW as the most positive peak within the 430–700-ms window following the P3. For statistical comparison of the latencies of the two ERP components, a 2-way ANOVA with factors Task and Condition (match vs. non-match) was applied. The amplitudes of the ERP components were analyzed using a 3-way ANOVA with the factors being Task, Condition and Electrode (15 sites).

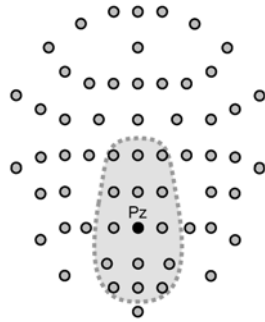


Fig. 4.4.2. The 15-electrode set for the analysis of the P3 and PSW.

Source configurations underlying the MEG data sets were modeled using the minimum-current estimate (MCE) algorithm (Uutela et al., 1999). MCEs for all experimental conditions were calculated separately for each individual subject. Averaged responses were preliminarily filtered with a 20-Hz low-pass digital filter. Detrended baseline was set at an 800 – 1000-ms time interval in order to eliminate low-frequency noise. Computations were performed for each time sample starting from 100 ms before and up to 1000 ms after the stimulus onset using the spherically symmetric conductor model with the origin determined individually for each subject on the basis of his/her anatomical MRI. The brain volumes with the highest current amplitudes within the region of interest were selected manually. Their extent and coordinates of their center were adjusted automatically to the maximal activity. The time courses of the activity within the selected areas were automatically calculated as a spatially weighted average of the estimate with the maximal weight at the center of the volume. Two consecutive 150-ms integration windows, chosen individually based on the global field power plots, were used for the analysis of both slow responses, the P3 and PSW. The same windows were always used for all conditions within the individual data set. For the statistical analysis, the averaged amplitudes across the 150-ms time windows were compared between the tasks, the probe types (match vs. non-match), hemispheres, and the two components (P3 vs. PSW). The source locations were transformed to the ICBM 152 standard coordinate space.

Statistical analysis of the behavioral data (accuracy and subjective difficulty level) was performed using the paired nonparametric Wilcoxon’s signed-ranks test. Reaction times were analyzed using a 2-way ANOVA with the factors being Task and Probe Type. Post-hoc analyses were performed using the Newman–Keuls test.

In all studies, after the experiment, the subjects were asked to fill a questionnaire and indicate, on a five-point scale, the subjective difficulty level of the tasks (1 = very easy, 2 = easy, 3 = intermediate, 4 = difficult and 5 = very difficult). They also described the strategies they had used during task performance by choosing the most appropriate definition from a list of five alternatives (“auditory rehearsal”, “verbal”, “visual imagery”, “somato-sensory imagery” and “no certain strategy”).

4.5. Summary of methods

Study	Sub-jects	Paradigm	Stimuli	Localiz. cue	Method	Response of interest
I	12	Loc & Pitch, 1-back & 2-back	Same for both tasks: 3 freq. (1000, 2250, 3375 Hz) & 3 loc. (L, M, R)	IID (17 dB)	Behavioral	Behavioral
II	11	Loc & Pitch, 1-back & 3-back	Loc: L, M, R (2250 Hz) Pitch: 1000, 2250, 3375 Hz (M)	IID (17 dB)	EEG (21 site)	Late slow waves
III	11	Loc & Pitch DMTS	Same for both tasks: 2 freq. (1000, 1500 Hz) & 2 loc. (L, R)	IID (17 dB)	EEG (64 sites) MEG (122 ch.)	N1 / N1m
IV	19	Loc & Pitch 3-back/DMTS	Same for both tasks: 3 freq. (220, 440, 880 Hz) & 3 loc. (L, M, R)	IID (13 dB)	EEG (60 sites) MEG (306 ch.)	Transient and slow components
V	19			+ ITD (500 μ s)	T1-MRI	P3 and PSW

Table 1. Summary of methods.

L – left; M – middle; R – right; IID – interaural intensity difference; ITD – interaural time difference DMTS – delayed matching-to-sample.

5. RESULTS

Study I. Effect of selective interference on auditory working memory processing

Effect of load. Memory load had a significant main effect on accuracy of task performance ($F(1,11) = 11.48, p < 0.05$), reaction times ($F(1,11) = 16.25, p < 0.005$) and subjective difficulty level ($F(1,11) = 40.26, p < 0.005$). Subjects made significantly more incorrect responses and had longer reaction times (RTs) in the 2-back than in the 1-back tasks which were also evaluated as more difficult (Fig. 5.1, A, B, C).

General effect of distraction. In 1-back tasks subjects made more incorrect responses in the distraction than normal conditions ($F(2,22) = 9.03, p < 0.05$), while in 2-back tasks distracters significantly shortened reaction times ($F(2,22) = 7.33, p < 0.05$). At both memory loads, distraction conditions were considered more difficult than the corresponding normal conditions ($F(2,22) = 34.40, p < 0.005$ for 1-back and $F(2,22) = 100.33, p < 0.005$ for 2-back) (Fig. 5.1, C).

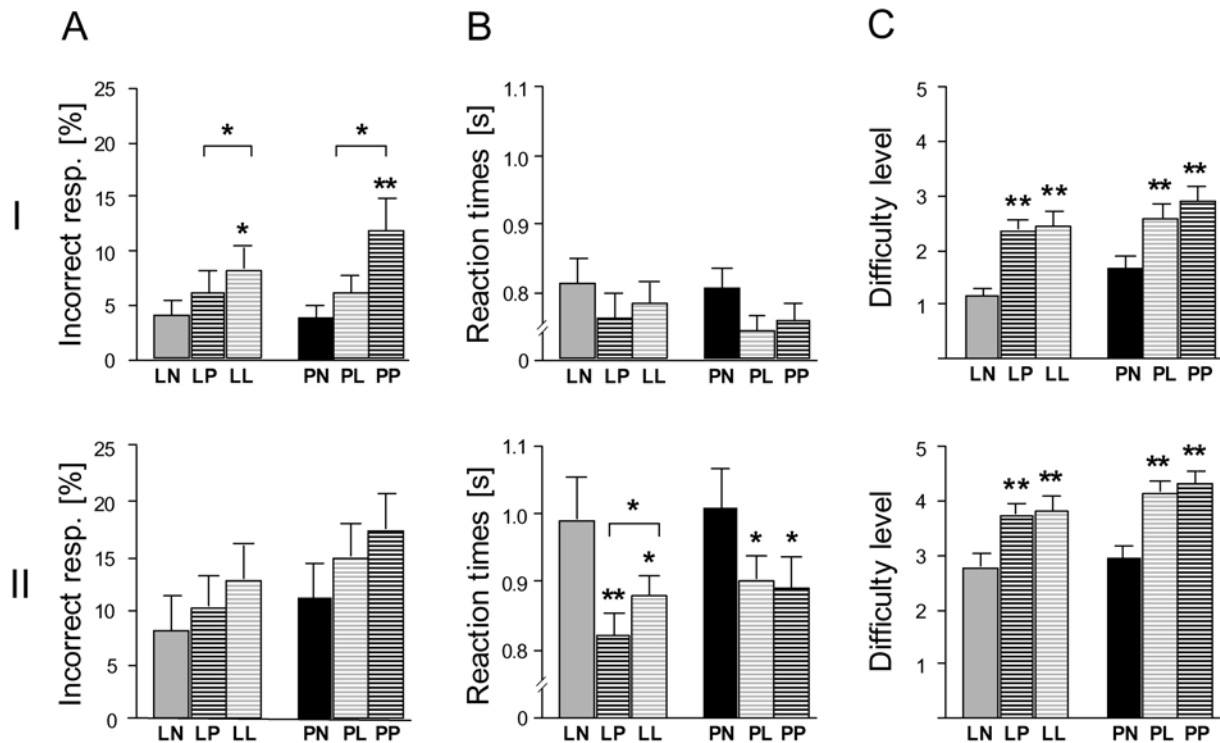


Fig. 5.1. The mean percentages of incorrect responses (A), the mean reaction times (B) and the mean subjective difficulty levels (C) in the 1-back (I) and 2 - back (II) location and pitch tasks. The vertical lines indicate standard errors of mean (SEM). LN = normal location task, LL = location task with location distracters, LP = location task with pitch distracters, PN = normal pitch task, PL = pitch task with location distracters, PP = pitch task with pitch distracters. The asterisks indicate the difference between the distraction and the corresponding normal condition, and when above a bracket, between two distraction conditions. * $p < 0.05$, ** $p < 0.005$

Effect of task. The type of task did not affect significantly either task performance (RTs and accuracy) or subjective evaluation of task difficulty. The most important finding of Study I was a significant effect of task and condition interaction on the number of incorrect responses at the low memory load ($F(2,22) = 8.69, p < 0.005$). Both location and pitch 1-back task performances were selectively disrupted by the distracters qualitatively similar to the memoranda ($p < 0.05$ for the location and $p < 0.005$ for the pitch task respectively). Furthermore, there was a significant difference between the two distraction conditions in both tasks ($p < 0.05$) (Fig. 5.1, A). At the high memory load (2-back), interaction between task and condition significantly affected the RTs ($F(2,22) = 3.55, p < 0.05$). In the location but not in the pitch task, the RTs were longer in the location than pitch distraction condition ($t(11) = 3.42, p < 0.05$) (Fig. 5.1, B).

In the 1-back pitch task, most of the subjects ($n=9$) reported having used an auditory rehearsal strategy, two had used a verbal, and one a visual strategy. In the 1-back location task, three subjects had used an auditory rehearsal strategy, three verbal, two visual, and four subjects a spatial strategy. In the 2-back pitch task, as in the 1-back task, most of the subjects ($n=8$) had used an auditory rehearsal strategy, two subjects a verbal, and two a visual strategy. In the 2-back location task, only one subject had used an auditory rehearsal strategy, three a verbal, three a visual, and the rest of subjects ($n=5$) a spatial strategy.

Study II. Effect of memory load and auditory stimulus attribute on the cortical distribution of late slow waves

Behavioral data. The number of incorrect responses was significantly affected by both memory load ($F(1,10)=14.79, p < 0.005$) and type of task ($F(1,10)=10.27, p < 0.01$). The interaction between the task and load was also significant ($F(1,10)=15.94, p < 0.005$). The subjects made more incorrect responses both in the location ($p < 0.01$) and pitch ($p < 0.005$) 3-back tasks than in the corresponding 1-back tasks (Fig. 5.2). The 3-back pitch task induced more incorrect responses than the 3-back location task ($p < 0.005$) but the respective difference between the 1-back tasks was not significant.

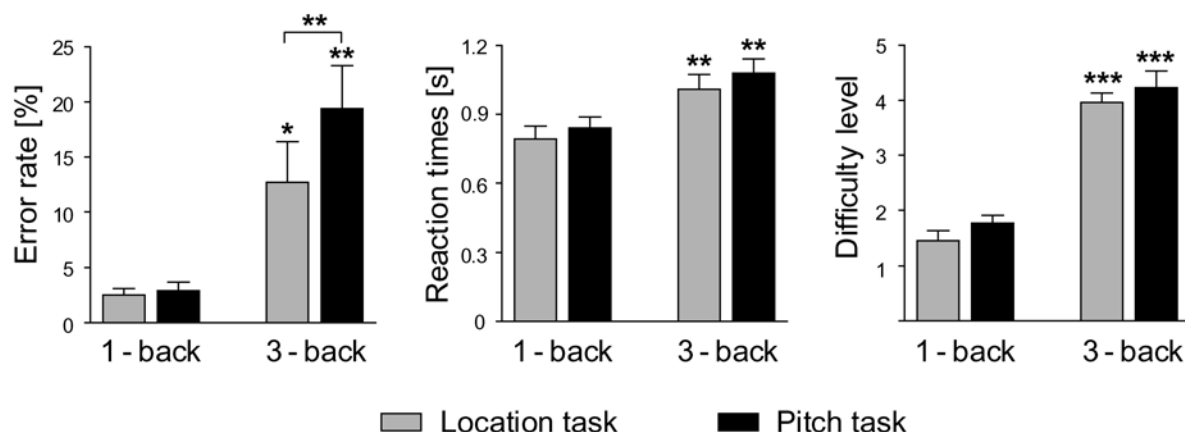


Fig. 5.2. The mean percentages of incorrect responses, the mean reaction times and the mean subjective difficulty levels in the 1- and 3 - back location and pitch tasks. The vertical lines indicate SEM. The asterisks indicate the difference between the high-load and the corresponding low-load condition, and when above a bracket, between two tasks, * $p < 0.05$, ** $p < 0.005$, *** $p < 0.001$

The RTs were affected by load ($F(1,10)=42.01$, $p < 0.005$) but not by task. The RTs were significantly longer both in the location ($p < 0.005$) and pitch ($p < 0.005$) 3-back tasks than in the corresponding 1-back tasks. Subjective evaluation of the difficulty level was dependent on memory load ($F(1,10)=111.45$, $p < 0.001$) but not type of task. Most of the subjects used a visual rehearsal strategy both in the pitch ($n=6$) and location ($n=7$) tasks. The rest of the subjects verbalized the stimuli, used an auditory rehearsal strategy, or reported that they had used no particular strategy during the task performance.

Late slow waves. Mnemonic load but not type of task (Fig. 5.3) had a significant main effect on the amplitude of the slow potential at the early phase (700-1400 ms) of the delay ($F(1,10)=6.06$, $p < 0.05$). The post-hoc test revealed that this difference was significant over the parietal-occipital matrix ($p < 0.05$) while in the frontal matrix there was no significant effect of load on the amplitude of slow potentials at any phase of the delay.

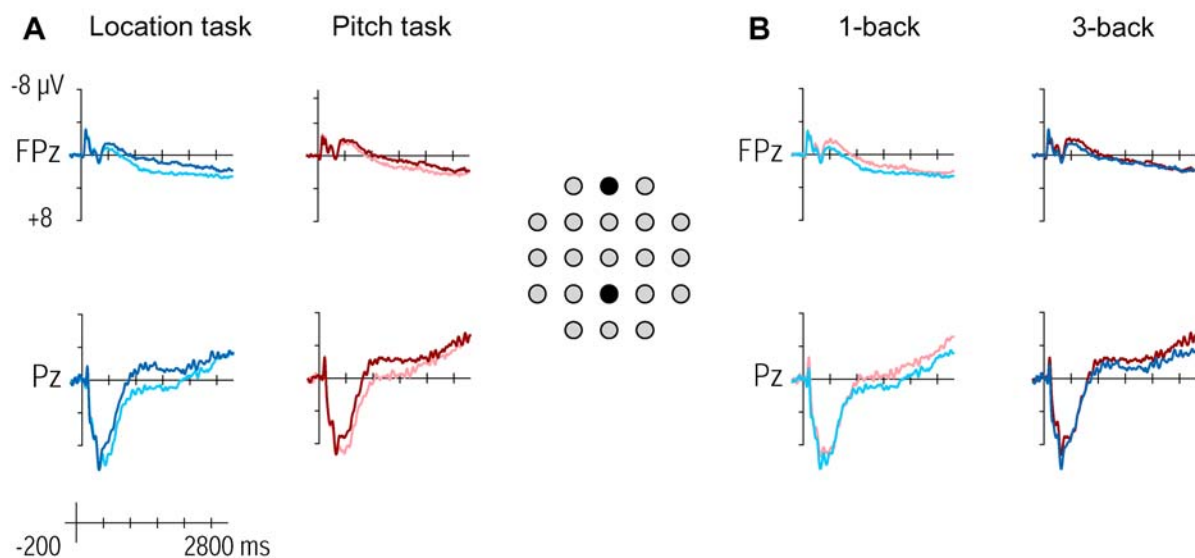


Fig. 5.3. The effect of memory load on the amplitude of LSW. (A) Superimposed grand-averaged waveforms recorded during low- and high-load conditions of location (left column) and pitch (right column) tasks at FPz (upper row) and Pz (lower row) recording sites. (B) Superimposed grand-averaged waveforms recorded during location and pitch tasks at FPz (upper row) and Pz (lower row) recording sites across the two memory loads. Light colours = 1-back task, dark colours = 3-back. Blue colour scale = Location task, red colour scale = Pitch task.

Study III. Effect of the auditory stimulus attribute on the electric and magnetic counterparts of the auditory N1

Behavioral data. Analysis of the behavioral data revealed a significant difference in reaction times (RTs) between the location and pitch tasks (Fig. 5.4): the subjects responded significantly faster during location task performance ($p < 0.01$). The RTs were 639 ± 70 ms (mean \pm standard error of mean, SEM) for the location task and 685 ± 72 ms for the pitch task. However, there was no significant difference in the task performance accuracy during location and pitch tasks. The percentage of incorrect responses was 3.3 ± 1.2 for the location

task and 3.9 ± 2.0 for the pitch task. There was no significant difference between the evaluations of the subjective difficulty level of the tasks. The score was 1.8 ± 0.2 for the location and 2.0 ± 0.2 for the pitch task, corresponding to the "easy" level of difficulty. In the pitch task, 9 out of the 11 subjects reported having used an auditory rehearsal strategy, one used visual imagery and one reported having used no any particular strategy. In the location task, 7 subjects used an auditory rehearsal strategy, one a visual, one a somato-sensory, and one a verbal strategy; one subject reported not having used any strategy.

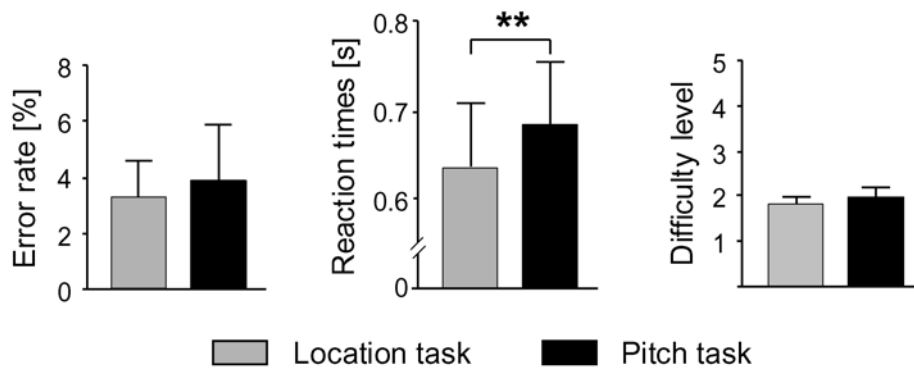


Fig. 5.4. The mean percentages of incorrect responses, the mean reaction times, and the mean subjective difficulty levels in the location and pitch tasks. The vertical lines indicate SEM, ** $p < 0.01$

EEG data. In both tasks, tones elicited clear ERPs containing N1, P2, N2 and P3 components (Fig. 5.5, B) with typical scalp distributions: fronto-central for N1, central for P2, frontal for N2 and parietal for P3. The peak latencies and amplitudes of these components at the representative sites, where the components were maximal, are given in Table 5.1.

Peak latencies of ERP components: The type of task had a significant main effect on the peak latency of N1 ($F(1,10)=6.50$, $p < 0.05$). Task and condition interaction was also significant ($F(2,20)=4.44$, $p < 0.05$). In the match condition the N1 latency was shorter in the location than pitch task ($p < 0.05$). This difference was significant at five out of the nine electrodes of the analyzed fronto-central set. The latency of the P2 component was significantly affected by the condition ($F(2,18)=4.97$, $p < 0.05$). In the match condition it was shorter than in both memory and non-match conditions ($p < 0.05$). Condition had also a significant effect on the latency of the N2 component ($F(2,18)=15.45$, $p < 0.001$): it was longest in the memory and shortest in the match condition.

Amplitudes of ERP components: Neither task nor condition had a significant effect on the amplitude of N1. Condition had a significant effect on the amplitude of P2 ($F(2,18)=4.67$, $p < 0.05$), which was significantly reduced in the match condition compared with the memory and non-match conditions ($p < 0.05$). The amplitude of the P2 was also significantly affected by the task and condition interaction ($F(2,18)=8.38$, $p < 0.01$): in the non-match condition it was higher during location than pitch task performance. The amplitude of the P3 component was significantly affected by condition ($F(2,18)=15.77$, $p < 0.001$): in the match condition it was higher than in memory ($p < 0.001$) and non-match ($p < 0.05$) conditions.

Component	Site	Task	Latency (ms)			Amplitude (μV)		
			Memory	Match	Non-match	Memory	Match	Non-match
N1	FCz	Location	93 ± 2	91 ± 3	95 ± 3	-6.0 ± 0.7	-5.9 ± 0.6	-5.6 ± 0.5
		Pitch	95 ± 2	98 ± 3	95 ± 2	-6.2 ± 0.7	-5.8 ± 0.6	-5.9 ± 0.6
P2	Cz	Location	193 ± 11	167 ± 9	187 ± 9	5.0 ± 0.4	3.2 ± 0.8	6.0 ± 0.7
		Pitch	198 ± 10	173 ± 8	189 ± 8	4.4 ± 0.5	3.8 ± 0.8	4.5 ± 0.5
N2	Fz	Location	293 ± 9	226 ± 16	254 ± 11	-0.4 ± 0.3	-1.1 ± 0.5	0.1 ± 0.4
		Pitch	287 ± 11	239 ± 12	259 ± 11	-0.7 ± 0.3	-1.0 ± 0.5	-0.7 ± 0.5
P3	Pz	Location	312 ± 13	341 ± 8	332 ± 13	3.4 ± 0.4	7.0 ± 0.7	5.9 ± 0.8
		Pitch	323 ± 16	341 ± 7	334 ± 14	3.1 ± 0.3	6.7 ± 0.7	5.1 ± 0.7

Table 5.1. Mean peak latencies and amplitudes (\pm standard error of the mean, SEM) of the electric components of auditory ERPs elicited during location and pitch task performance.

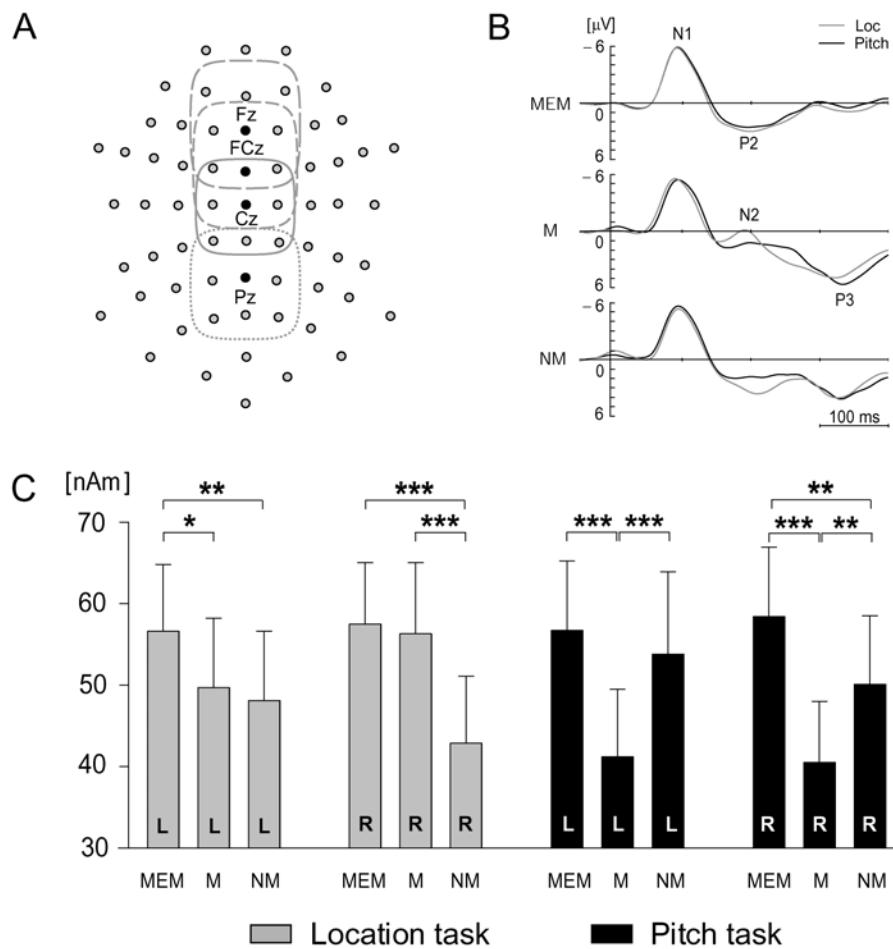


Fig. 5.5. (A) The 9-electrode sets for the analysis of ERP components: frontal (for N2), fronto-central (for N1), central (for P2) and parietal (for P3). Filled circles indicate representative sites. (B) Grand-averaged waveforms recorded at the fronto-central electrode site (FCz) during memory (MEM), match (M) and non-match (NM) conditions of the location (grey line) and pitch (black line) task performance. (C) The effect of condition on the amplitude of the N1m component during location and pitch task performance. The vertical lines indicate SEM, $* = p < 0.05$, $** = p < 0.01$, $*** = p < 0.001$

MEG data. The N1m ECDs were reliably determined for all subjects in all experimental conditions. The mean goodness of fit was quite stable across experimental conditions, varying from $88 \pm 2\%$ to $93 \pm 2\%$ (Table 5.2).

Task	Condition	Left hemisphere			Right hemisphere		
		Latency (ms)	Amplitude (nAm)	Goodness of fit (%)	Latency (ms)	Amplitude (nAm)	Goodness of fit (%)
Location	Memory	98 ± 3	57 ± 8	92 ± 1	93 ± 2	57 ± 8	92 ± 2
	Match	96 ± 4	50 ± 9	90 ± 2	92 ± 3	56 ± 9	91 ± 2
	Non-Match	103 ± 3	48 ± 8	88 ± 2	92 ± 2	43 ± 8	90 ± 2
Pitch	Memory	97 ± 3	57 ± 8	93 ± 2	94 ± 2	58 ± 8	93 ± 1
	Match	102 ± 4	41 ± 8	89 ± 2	93 ± 2	41 ± 7	88 ± 2
	Non-Match	103 ± 3	54 ± 10	90 ± 2	92 ± 3	50 ± 8	89 ± 1

Table 5.2. Mean amplitudes, latencies and goodness of fit (\pm SEM) of the ECDs determined for the N1m component of the auditory ERPs elicited during location and pitch task performance.

N1m latencies: Neither task nor condition had a significant main effect on the latency of the magnetic counterpart of N1 (N1m). However, similarly to the electric N1 latency, the latency of N1m also tended to be affected by task in the match condition. The mean latency of the N1m in the left hemisphere was 6 ms shorter in the location than pitch task (Table 5.2), which was comparable with the task-related N1-latency difference found in the match condition at the fronto-central electrode site. The N1m latency was significantly affected by hemisphere ($F(1,10)=8.56, p < 0.05$). It was shorter in the right than left hemisphere in all experimental conditions.

N1m amplitudes: Distributions of the N1m amplitudes across experimental conditions are shown in Fig. 5.5, C. As the figure clearly shows, the amplitude of the N1m was significantly affected by the experimental condition ($F(2,20)=6.27, p < 0.05$). In both location and pitch tasks, the ECD amplitudes were maximal in the memory condition in both hemispheres. Task and condition interaction also produced a significant effect on the N1m amplitude ($F(2,20)=15.26, P < 0.001$). Task-related differences between ECD amplitudes were obtained in the match and non-match conditions. In the match condition, the ECD amplitude was significantly larger during location than pitch task performance in the left ($p < 0.01$) and right ($p < 0.001$) hemispheres. In the non-match condition, the ECD amplitudes in both hemispheres were significantly higher during pitch than location task performance ($p < 0.05$, left hemisphere, and $p < 0.01$, right hemisphere). In the location task, the ECD amplitude was highest in the memory condition and lowest in the non-match condition. In the pitch task, however, the highest amplitude of the N1m was also observed in the memory condition, while the lowest – in the match condition (level of statistical significance for the N1m amplitude differences between experimental conditions is shown in the figure).

N1m source coordinates: Analysis of the ECD coordinates revealed a significant effect of the task and condition interaction on the location of the N1m generator along the x axis

($F(2,20)=9.01, p < 0.01$). Mean coordinate values and their standard errors are given in Table 5.3. The source of the N1m determined in the match condition of the location task in the right hemisphere was situated significantly medially to the sources of the N1m components elicited in all other experimental conditions ($p < 0.05$). In the match condition, the N1m ECD in the location task was located medially to the corresponding N1m ECD in the pitch task in all 11 subjects.

Task	Condition	Left hemisphere			Right hemisphere		
		<i>x</i>	<i>y</i>	<i>z</i>	<i>x</i>	<i>y</i>	<i>z</i>
Location	Memory	-46 ± 2	4 ± 3	58 ± 3	47 ± 2	13 ± 3	59 ± 3
	Match	-45 ± 2	4 ± 4	59 ± 3	44 ± 2	13 ± 3	60 ± 3
	Non-Match	-47 ± 2	3 ± 4	61 ± 3	49 ± 3	13 ± 3	61 ± 3
Pitch	Memory	-46 ± 2	3 ± 4	57 ± 3	49 ± 2	12 ± 3	57 ± 3
	Match	-48 ± 2	3 ± 4	61 ± 3	49 ± 2	12 ± 3	59 ± 3
	Non-Match	-46 ± 3	5 ± 3	60 ± 2	47 ± 2	13 ± 3	58 ± 3

Table 5.3. Mean coordinate values (mm, \pm SEM) for the locations of the ECDs determined for the N1m component of the auditory ERPs elicited during location and pitch task performance.

There was a similar tendency in the differences between the *x*-coordinates of the ECDs determined in the left hemisphere. The ECD location was also significantly affected by hemisphere along the *y* axis ($F(1,10)=11.31, p < 0.01$). In the right hemisphere, ECDs were significantly anterior to the corresponding ECDs in the left hemisphere in all experimental conditions ($p < 0.001$) (Fig. 5.6).

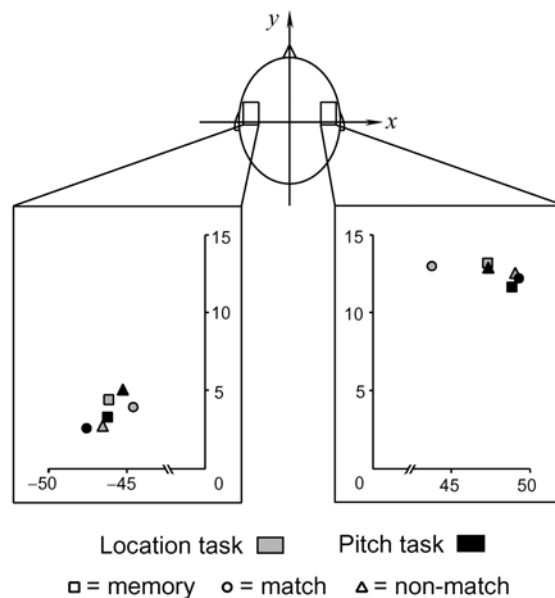


Fig. 5.6. Averaged locations of the ECDs, determined for the N1m in each experimental condition during location and pitch task performance (projection on the horizontal plane). □ = memory, ○ = match and △ = non-match conditions of the location (grey) and pitch (black) tasks.

Studies IV-V. Effect of memory load on electric and magnetic counterparts of auditory evoked responses recorded during spatial and nonspatial task performance

Behavioral data. Analysis of the behavioral data revealed no task-related differences either in the task performance or in the subjective evaluation of task difficulty (Fig. 5.7). Despite the rather complicated design, all 19 subjects managed to perform the task. The mean percentage of incorrect responses was 9.6 ± 1.7 (the mean \pm standard error of mean, SEM) for the location task and 10.2 ± 2.2 for the pitch task. The subjective difficulty level of both tasks was almost the same: 2.9 ± 0.2 for the location and 3.1 ± 0.2 for the pitch task, corresponding to the intermediate level. Reaction times did not differ significantly between the tasks but were significantly affected by the probe type. The reaction times in the match condition of both tasks were shorter than in the non-match condition ($p < 0.001$): 748 ± 46 ms. vs. 859 ± 47 ms. for the location task and 720 ± 39 vs. 818 ± 41 ms. for the pitch task. In the pitch task, seven subjects reported using an auditory rehearsal strategy, seven used a verbal strategy, three used visual and two somatosensory imagery. In the location task, only one subject reported using an auditory rehearsal strategy, nine used a verbal, five visual and four somatosensory imagery.

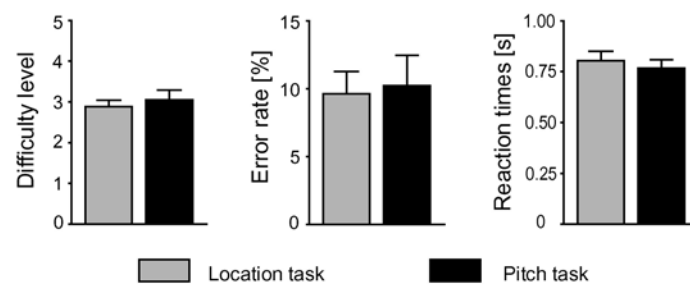


Fig. 5.7. Mean percentages of incorrect responses, mean reaction times and mean subjective difficulty levels obtained during the location and pitch tasks. The vertical lines indicate SEM, *** = $p < 0.001$.

Responses to memory cues (Study IV)

EEG data. Averaged auditory ERPs, recorded in both location and pitch tasks, contained N1, P2, N2 and P3 components, a parietal positive slow wave (PSW), and a late slow wave (LSW). The type of task affected the amplitude of the auditory ERPs at the latency of the N2 component, around 400 ms, and at the latency of the PSW. The magnitude of the LSW was affected by condition but not task. The peak latencies and amplitudes of the ERP components at the representative sites are given in Table 5.4.

Experimental condition significantly affected the peak latency of the N1 component ($F(2,36)=10.99$, $p < 0.001$): in cue I condition it was longer than in all other conditions. The amplitude of the N1 component was not affected either by task or condition.

The type of task had a significant main effect on the amplitude of the N2 component ($F(1,18)=5.47$, $p < 0.05$): in the pitch task it was higher than in the location task. Condition had a significant effect on the latency of the N2 component ($F(2,36)=9.50$, $p < 0.01$). In cue I

condition it was longer than in cue II and cue III conditions ($p < 0.01$). Condition also affected the amplitude of the N2 component ($F(2,36)=3.96, p < 0.05$). In cue I condition it was higher than in cue II and cue III conditions ($p < 0.05$).

Neither task nor condition affected the latency of the P3 component, but its amplitude was significantly affected by condition ($F(2,36)=29.25, p < 0.001$). There was a gradual increase in the amplitude of the P3 from cue I to cue III condition ($p < 0.001$ for all changes).

ERP component	Site	Task	Latency (ms)			Amplitude (μ V)		
			Cue I	Cue II	Cue III	Cue I	Cue II	Cue III
N1	FCz	Loc.	98 \pm 2	95 \pm 3	94 \pm 3	-6.8 \pm 0.8	-6.7 \pm 0.6	-6.8 \pm 0.6
		Pit.	98 \pm 2	95 \pm 3	95 \pm 2	-6.4 \pm 0.7	-6.3 \pm 0.6	-6.7 \pm 0.6
P2	Cz	Loc.	188 \pm 5	186 \pm 5	184 \pm 5	5.1 \pm 0.6	5.6 \pm 0.6	5.8 \pm 0.5
		Pit.	191 \pm 4	184 \pm 4	183 \pm 4	5.5 \pm 0.6	5.2 \pm 0.6	5.3 \pm 0.5
N2	Fz	Loc.	286 \pm 8	270 \pm 7	262 \pm 8	-1.1 \pm 0.7	0.3 \pm 0.5	0.2 \pm 0.6
		Pit.	282 \pm 7	270 \pm 6	263 \pm 7	-1.6 \pm 0.8	-0.7 \pm 0.5	-0.5 \pm 0.5
P3	CPz	Loc.	359 \pm 12	348 \pm 11	345 \pm 11	3.6 \pm 0.6	5.0 \pm 0.5	6.7 \pm 0.6
		Pit.	359 \pm 14	335 \pm 8	335 \pm 8	2.6 \pm 0.6	4.6 \pm 0.4	6.0 \pm 0.5
400 ms	Cz	Loc.	408 \pm 6	409 \pm 8	405 \pm 6	1.1 \pm 0.7	2.5 \pm 0.5	3.4 \pm 0.6
		Pit.	414 \pm 5	411 \pm 5	413 \pm 5	-0.4 \pm 0.6	1.0 \pm 0.6	1.9 \pm 0.7

Table 5.4. Mean peak latencies and amplitudes (\pm SEM) of the ERP components elicited during location and pitch task performance at representative sites.

The most prominent amplitude difference between the ERPs recorded during the two tasks was observed at the latency of about 400 ms in all cue conditions (Fig. 5.8, A) at the central – centro-parietal recording sites (Fig 5.8, D). This finding led us to further analyze the negative-going deflection of the ERPs separating the P3 component and PSW. This deflection was analyzed within a time window of 330–480 ms (amplitude integration 30 ms around the peak) in the central 9-electrode set. The amplitude of this peak was significantly affected by the type of task ($F(1,18)=16.8, p < 0.001$), being more negative during the pitch than location task. Its latency, however, was not affected either by task or condition.

The mean amplitude of the PSW measured between 450 and 650 ms over the parietal electrode sites was significantly affected by condition ($F(2,36)=32.26, p < 0.001$). It increased gradually with the memory load ($p < 0.001$ for all changes) (Fig. 5.8, B). Furthermore, there was an effect of task and condition interaction on the amplitude of the PSW ($F(2,36)=4.01, p < 0.05$). A significant task-related difference was found in cue I condition only: the amplitude of the PSW was higher in the location than pitch task ($p < 0.001$) (Fig. 5.8, C). The amplitude maximum of this task-related difference was over the parietal – parieto-occipital sites (Fig. 5.8, D).

Thus, significant task-related amplitude differences in the auditory ERPs occurring at the time range of the N2 component and at the latency of about 400 ms did not vary as a function of memory load. However, the amplitude difference at the latency of the PSW was load-dependent: it decreased with increasing number of items to be retained.

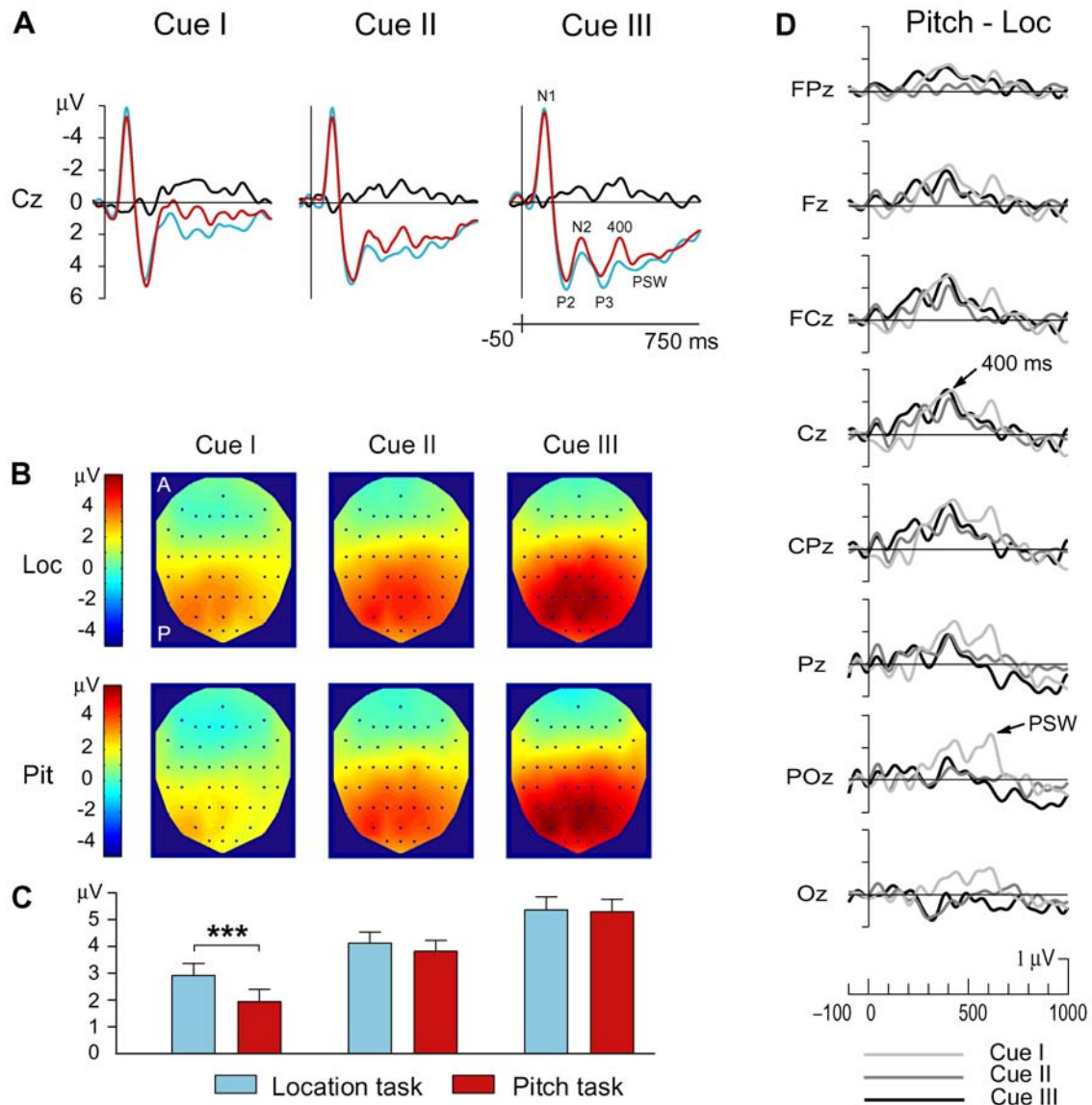


Fig. 5.8. (A) Grand-averaged waveforms recorded at the Cz electrode site during three cue conditions of location (blue) and pitch (red) tasks. Black lines represent difference waves (Pitch minus Location). (B) Spatial distribution of mean amplitudes of the PSWs recorded during the three cue conditions of location (Loc) and pitch (Pit) tasks averaged within 450-650 ms time window; A – anterior, P – posterior. (C) The mean amplitudes of the PSWs obtained during the three cue conditions of location (blue bars) and pitch task (red bars). The vertical lines indicate SEM, *** = $p < 0.001$. (D) Superimposed grand-average difference waves (Pitch minus Location) obtained in the three cue conditions at midline recording sites. Negativity is plotted upwards. Arrows indicate deflections corresponding to task-related differences at the latency around 400 ms and during the PSW.

The amplitudes of the LSW were significantly affected by the memory load in both frontal ($F(2,36)=5.43, p < 0.05$) and parietal ($F(2,36)=6.20, p < 0.01$) arrays of electrodes (Fig. 5.9, A, D). In the frontal array, the mean amplitude of the slow waves was highest in cue I condition and differed significantly from the slow wave amplitudes in the other cue conditions ($p < 0.05$). Over parietal areas, the most prominent slow waves were recorded in cue III condition. Their magnitudes differed significantly from the magnitudes of the slow waves recorded in both cue I ($p < 0.01$) and cue II ($p < 0.05$) conditions (Fig. 5.9, C). Although the

amplitude of the slow waves increased gradually from cue I to cue III condition, this increase was not significant between cue I and cue II condition. The type of task did not affect the amplitudes of the LSW in either frontal or parietal arrays of channels (Fig. 5.9, B).

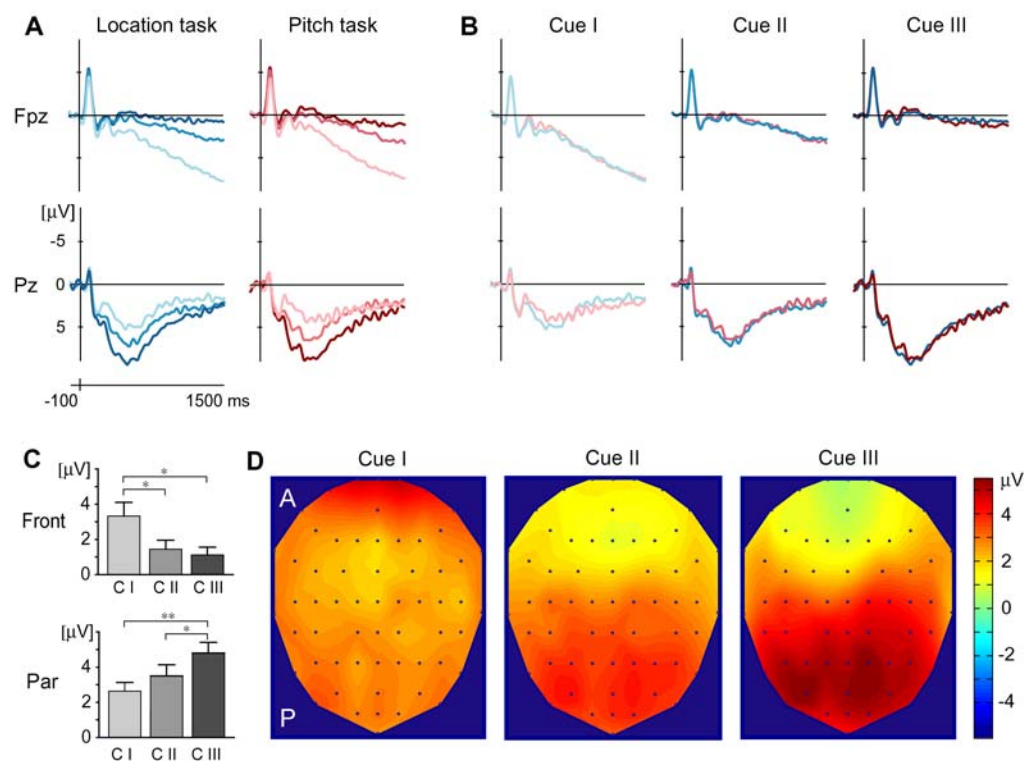


Fig. 5.9. The effect of memory load on the amplitude of LSW. (A) Superimposed grand-averaged waveforms recorded during the three cue conditions of location (left column) and pitch (right column) tasks at Fpz (upper row) and Pz (lower row) recording sites. Lightest colours = Cue I, darkest colours = Cue III. Blue colour scale = Location task, red colour scale = Pitch task. (B) Superimposed grand-averaged waveforms recorded during location and pitch tasks at Fpz (upper row) and Pz (lower row) recording sites across the three cue conditions (from left to right column). Blue colour scale = Location task, red colour scale = Pitch task. (C) The mean amplitudes of the LSWs obtained during the three cue conditions within frontal (Front) and parietal (Par) electrode-arrays. The vertical lines indicate SEM, * = $p < 0.05$, ** = $p < 0.01$. (D) Spatial distribution of mean amplitudes of the LSWs recorded during the three cue conditions averaged within a 500-1500-ms time window.

MEG data. The type of task affected both the latency and source location of the N1m component of the auditory responses. Bilateral equivalent current dipoles (ECDs) were determined for the N1m component with the mean value of the goodness of fit varying from $88 \pm 1\%$ to $92 \pm 1\%$ (mean \pm standard error of mean, SEM) between experimental conditions. The latency of the N1m component was shorter during the location than the pitch task performance ($F(1,16)=8.42$, $p < 0.05$). Condition had also a significant main effect on the N1m latency ($F(2,32)=7.28$, $p < 0.01$). In cue I condition it was significantly longer than in the other conditions. The N1m latency was also affected by the task and condition interaction ($F(2,32)=6.40$, $p < 0.01$). It was shorter in the location than pitch task across all cue conditions, but the task-related difference was statistically significant only in cue III condition ($p < 0.001$). The amplitude of the N1m was significantly affected by condition ($F(2,32)=3.95$,

$p < 0.05$). In cue I condition the N1m amplitude was higher than in the other conditions ($p < 0.05$).

When the ECDs were laid over the individual MR images, the location of the N1m generators were in the vicinity of the Heschl's gyrus in all analyzed conditions. The coordinates of the ECDs were significantly affected by all main experimental factors: task (along z-axis, $F(1,16)=5.35$, $p < 0.05$), hemisphere (along y-axis, $F(1,16)=13.54$, $p < 0.01$) and condition (along x-axis, $F(2,32)=5.84$, $p < 0.01$). The generators of the N1m component were situated significantly more superiorly in the pitch than location task, more laterally in cue I than in the other conditions, and more frontally in the right than left hemisphere (Fig. 5.10, A, B).

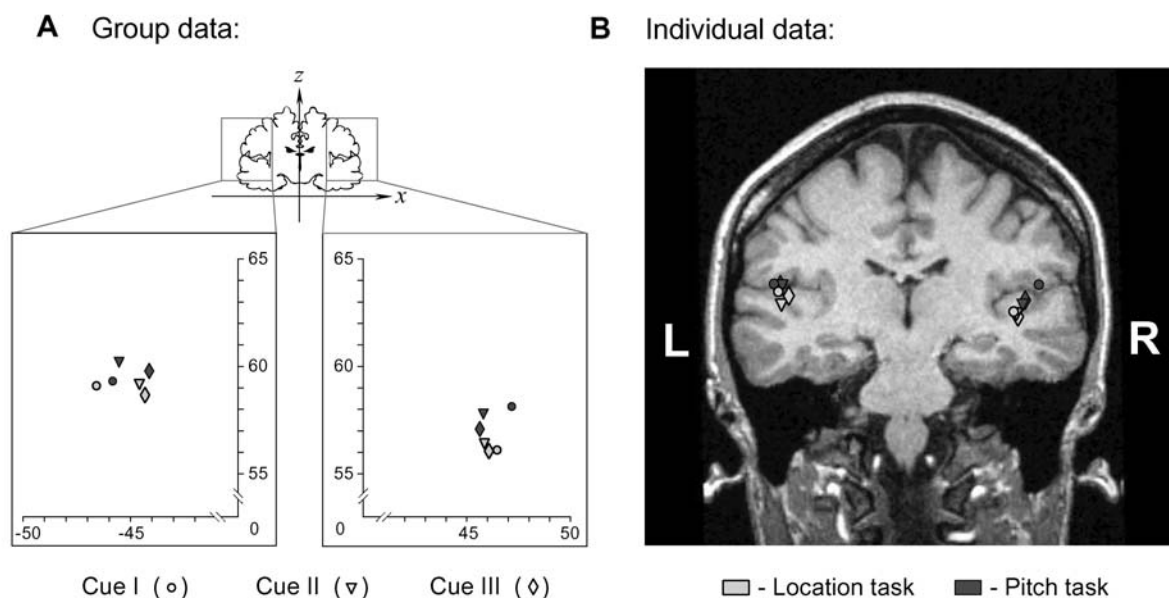


Fig. 5.10. Averaged locations of the ECDs determined for the N1m in the three cue conditions during Location (grey) and Pitch (black) task performance (projection on the coronal plane). (B) Data from an individual subject overlaid on his T1-weighted MR image.

Responses to probes (Study V)

EEG data. The P3 and PSW appeared as separate peaks in 16 out of 19 subjects in all experimental conditions. In three subjects, these components were completely merged at least in one condition, which made it impossible to include their data in the group statistics.

The main finding from the EEG data was a prominent and differential effect of the probe type on the amplitudes of both the P3 and the PSW (component and condition interaction, $F(1,15)=50.5$, $p < 0.001$). The amplitude of the P3 was higher in the match than non-match condition ($p < 0.01$), while the PSW was higher in the non-match than match condition ($p < 0.001$) (Fig. 5.11, A, B, C). However, the latencies of the P3 and PSW components did not depend on the probe type and were not significantly different in the match and non-match conditions. The type of task (location or pitch) did not affect the amplitudes or latencies of the slow positive components of the auditory evoked responses to probes.

As expected, the P3 and PSW amplitudes were significantly affected by the electrode site ($F(14,210)=13.9$ and $F(14,210)=20.4$ respectively, $p < 0.001$). There were slight differences in the scalp distributions of the P3 and PSW: the maximum values of the P3 amplitudes were obtained at the parietal electrodes while the amplitude maximum of the PSW was focused at the parieto-occipital electrodes. The late positive components were found to correlate with the behavioral data. The amplitudes of both the P3 and PSW correlated negatively with RTs, suggesting enhancement of the late positive components when the responses were faster. Pearson correlation coefficient was -0.67 ($p < 0.001$) for the P3 recorded at Pz site and -0.46 ($p < 0.001$) for the PSW at POz site. The latency of the PSW correlated positively with RTs (Pearson correlation coefficient 0.39 , $p < 0.01$), whereas there was no correlation between the P3 latency and the efficiency of task performance.

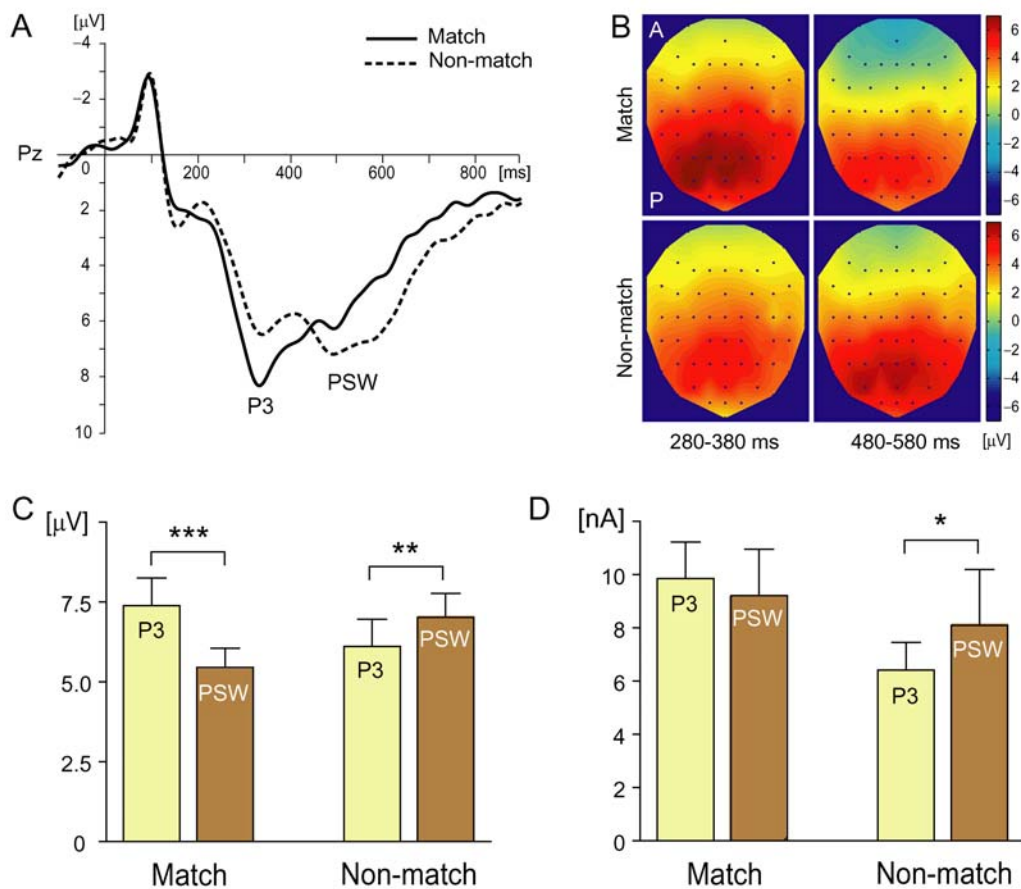


Fig. 5.11. The effect of the probe type on the amplitude of the slow endogenous components. (A) Grand-averaged waveforms recorded at the Pz electrode site during match and non-match conditions. (B) Spatial distribution of the mean amplitudes of the P3 (280–380 ms) and PSW (480–580 ms) recorded during match and non-match conditions. (C) The mean amplitudes of the P3 and PSW within the analyzed electrode set. (D) Strength of magnetic field in the precuneal source. The vertical lines indicate standard errors of mean (SEM), * = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$.

MEG data. The minimum-current estimates suggested several areas as possible generators for the slow evoked responses: bilateral occipito-temporal (around the posterior part of the superior temporal sulcus (STS)), temporal (around the middle part of the STS) and parietal

(around the junction of the postcentral and intraparietal sulcus) cortices, and the precuneus (Table 1).

Interhemispheric differences. A clear interhemispheric difference was observed in the parietal source which was active mainly in the left hemisphere ($F(1,12)=16.6, p < 0.01$). The amplitude of the temporal source was higher in the right hemisphere ($F(1,12)=6.9, p < 0.05$).

Match versus non-match: effect of probe type. The Probe type significantly affected the amplitudes of the evoked responses in the parietal ($F(1,12)=7.2, p < 0.05$) and precuneal ($F(1,13)=4.8, p < 0.05$) sources: both exhibited higher activity in the match than non-match condition. Furthermore, the activity of the precuneal source was affected by the Probe type and Component interaction ($F(1,13)=4.6, p = 0.05$): in the non-match condition the amplitude of the evoked field was higher during PSW than during P3 (Fig. 5.11, D).

Differences between components. Both the temporal ($F(1,12)=21.8, p < 0.001$) and occipito-temporal ($F(1,8)=11.2, p < 0.05$) sources were significantly affected by the component. While the occipito-temporal source demonstrated higher activity during the generation of the P3, the activity in the temporal source was higher at the PSW than at the preceding P3 (Fig. 5.12, A, B).

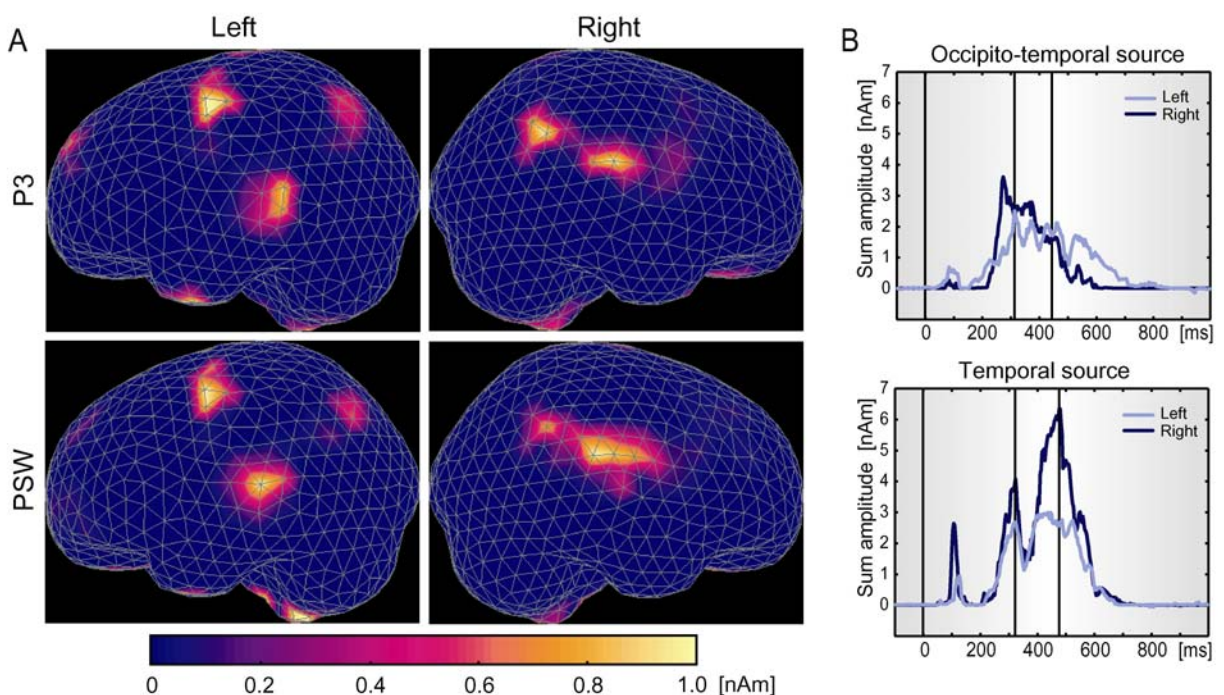


Fig. 5.12. Interhemispheric differences in the spatial distribution of the sources of the late endogenous components. (A) Grand average minimum-current estimate (MCE) source locations of the P3 (upper row) and PSW (lower row) in the left and right hemispheres. (B) Grand average activation time courses of the temporal (upper panel) and occipito-temporal (lower panel) sources.

Location versus pitch: the effect of task. The occipito-temporal and temporal generators of the slow evoked responses were sensitive to the Type of task. The occipito-temporal source of the P3 demonstrated higher activity in the location than pitch task (Task and Component interaction, $F(1,8)=8.5, p < 0.05$). Moreover, there was a structural segregation in the coordinates of the center of the active area in the medio-lateral direction. In the location task,

the right-hemispheric occipito-temporal source was situated 5 mm more medially than in the pitch task ($F(1,5)=10.2, p < 0.05$) (Fig. 5.13, A, B).

There was some indication that activity in the temporal source also varied as a function of task type. In the analysis of the temporal source activity, the Hemisphere, Task and Component interaction was not, however, quite significant ($F(1,12)=4.0, p < 0.07$). The activity in the left temporal generator of the PSW tended to be stronger during the pitch than location working memory task. The planned comparison revealed a significantly higher activity in the left temporal generator of the PSW during the pitch than location working memory processing ($p < 0.01$).

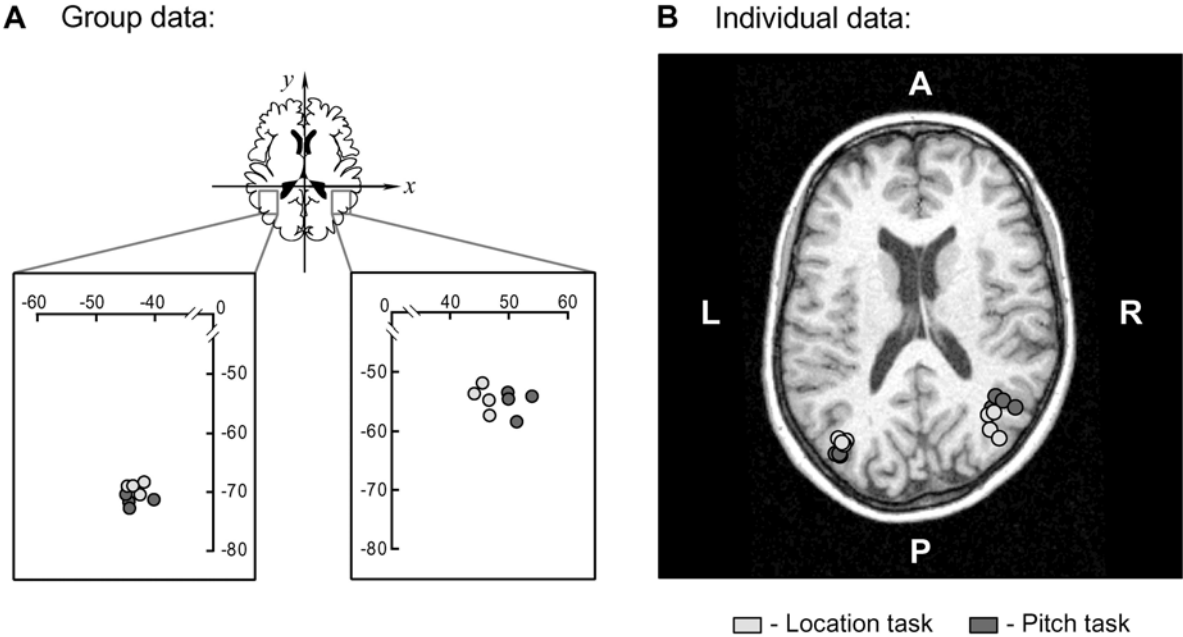


Fig. 5.13. The effect of sound attribute on the spatial location of the occipito-temporal source. (A) Averaged Talairach coordinates of the occipito-temporal generator of late endogenous components (projection on the axial plane). (B) Sources of the P3 and PSW recorded during match and non-match conditions of the location (grey circles) and pitch task performance (black circles). Data from an individual subject overlaid on his T1-weighted MR image.

6. DISCUSSION

The main purpose of the present Ph.D. project was to test the hypothesis of segregation of spatial and nonspatial auditory information processing at behavioral level and by recording the electrophysiological evoked responses during working memory task performance.

6.1. Evidence for dissociation between spatial and nonspatial auditory information processing obtained at the behavioral level (Study I)

The main finding of the first study was that distractors qualitatively similar to the memoranda caused interference on the accuracy of task performance. This finding is in line with previous behavioral experiments on the effect of selective interference in the auditory (Deutsch, 1970; Clarke et al., 1998) and visual working memory tasks (Vuontela et al., 1999). Study I extends the results from earlier behavioral studies in the auditory modality by demonstrating a double dissociation in the effects of selective auditory distraction on spatial and nonspatial auditory working memory task performance. However, a double dissociative effect on spatial and nonspatial task performance was obtained only at the low memory load level (1-back task), while the 2-back tasks were not significantly disrupted by either type of interference. This finding suggests that the dissociative effect of the selective interference is memory load-dependent. In several electrophysiological (Ruchkin et al., 1992) and neuroimaging studies (Zatorre et al., 1994; Smith et al., 1995; Braver et al., 1997; Carlson et al., 1998; Martinkauppi et al., 2000), an increase in memory load has been shown to enhance task-related cortical activations. In accordance, the higher attentional and mnemonic demands of the auditory 2-back tasks may have recruited additional neuronal populations involved in both auditory location and pitch information processing, obscuring a dissociative effect of interference on the 2-back tasks. The lack of a dissociative effect of the selective interference on 2-back task performance may also be explained by the "self-distractive" nature of this task. Each new stimulus in the 2-back task has a dual role; it is a memorandum for the ongoing trial and a distractor for the previous one.

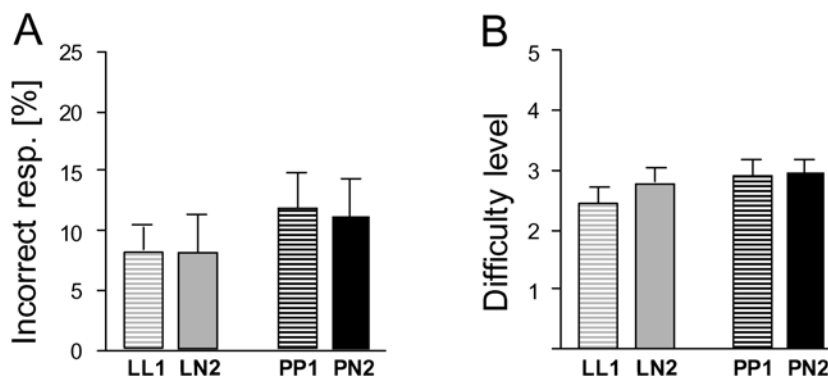


Fig. 6.1.1. Comparison of the mean percentages of incorrect responses (A) and subjective difficulty level (B) between the 1-back tasks with distractors qualitatively similar to the memoranda and the corresponding 2-back tasks without distractors. LL1=1-back location task with location distractors, LN2=2-back normal location task, PP1=1-back pitch task with pitch distractors and PN2=2-back normal pitch task.

As shown in Fig. 6.1.1, A, in the normal auditory 2-back tasks, the accuracy of performance was at the same level as in the corresponding auditory 1-back tasks with distractors qualitatively similar to the memoranda. Interestingly, the normal 2-back tasks were subjectively evaluated to be as difficult as the 1-back tasks with distraction (Fig. 6.1.1, B).

Thus, the results of Study I suggest that auditory working memory is segregated into spatial and nonspatial domains and that this segregation is memory load dependent.

6.2. Effect of memory load but not type of task on the Late Slow Waves (Studies II and IV)

The main finding of the second study was that memory load but not type of task modulated the amplitude of slow potentials recorded during spatial and nonspatial working memory tasks.

In functional magnetic resonance imaging (fMRI) studies, the *n*-back task has been shown to be a suitable tool for the detection of memory load-related brain activation (Braver et al., 1997; Carlson et al., 1998). In the *n*-back task, subjects respond after each stimulus and thus the movement related preparatory activity at different load levels is relatively constant from trial to trial. The stimulus presentation at different load levels is also constant and the number of items to be kept in mind varies only according to the instructions to perform the task. Thus it is likely that the amplitude difference in the Late Slow Waves (LSW) between 1-back and 3-back tasks was due to differences in the cognitive requirements, such as attention and memory, between the high- and low-load *n*-back tasks and not to neuronal processing related to movement execution.

On the other hand, the LSW recorded in Study II were insensitive to the type of task. One can, however, argue that motor-related activity, which was similar for both types of tasks, could mask the effect of the sound attribute on neuronal processing reflected in LSW. In a related study (Rämä et al., 2000), which is not included in the present thesis, the type of task did not affect the slow delay-related activity either in a matching-to-sample task in which the subjects were instructed to respond, by button pressing, only to the matching probes, and consequently did not know during the delay period whether to execute or inhibit the motor response.

The main finding of the second study was confirmed in Study IV, where a novel behavioral paradigm which enables the recording of memory-related responses that are not biased by a preparatory motor component was employed. The greatest effect of mnemonic load on LSW in Study IV was observed over frontal and parietal areas. The positivity of the LSW gradually decreased over the frontal recording sites with increasing memory load, whereas over the parietal sites it increased from cue I to cue III condition. Mnemonic load has been shown to modulate the LSW elicited both during visual and auditory task performance over frontal (Mecklinger and Pfeifer, 1996; Geffen et al., 1997; Rämä et al., 1997; McEvoy et al., 1998) and parietal (Mecklinger and Pfeifer, 1996; Martin-Loeches and Rubia, 1997; McEvoy et al., 1998) recording sites. The increase in the amplitude of parietal slow waves with increasing memory load is consistent with the view that growing task demands enhance the amplitude of

late slow potentials (Ruchkin et al., 1988). However, in Study IV, the LSW recorded over the frontal sites changed in the opposite direction. This suggests that frontal and parietal slow potentials elicited during the delay period of working memory tasks are functionally distinct and produced by different generators simultaneously involved in task performance.

In several studies, the enhancement of negativity of the LSW has been associated with temporal expectancy of a probe stimulus (e.g., Elbert et al., 1994; Starr et al., 1996). Thus modulation of the LSW over frontal areas across cue conditions may also be explained by overlap of memory-related and anticipatory neuronal activity. In contrast to memory load, the type of task did not affect LSW. This finding is also consistent with the results from earlier studies concerning visual modality (McEvoy et al., 1998). On the other hand, results from other studies on visual spatial and nonspatial working memory processing have demonstrated a clear difference between the amplitude and topography of parietal positive slow waves (Bosch et al., 2001) and late slow potentials recorded during nonspatial (object) and spatial task performance (Mecklinger and Pfeifer, 1996; Bosch et al., 2001). The amplitude and scalp distribution of slow waves have been shown to depend on the modality of the stimuli (Lang et al., 1992; Barcelo et al., 1997; Shubotz and Friderici, 1997). It is possible that in the visual system, working memory processing is more clearly dissociated into spatial and nonspatial domains, while in the auditory system there may be more overlap in the fronto-parietal networks involved in the retention of stimuli in working memory.

To conclude, Studies II and IV did not show any dissociation between auditory spatial and nonspatial information processing at the time range of the Late Slow Waves.

6.3. Effect of task on transient auditory evoked responses: electrophysiological evidence for dissociation between spatial and nonspatial auditory information processing

6.3.1. The N1 component in the matching-to-sample task (Study III).

Study III was the first attempt to test the suggestion that the dissociation between “what” and “where” processing in the auditory system may take place at time range of transient evoked responses preceding LSW. Spatial and nonspatial delayed matching-to-sample tasks were employed. The experimental paradigm was designed so that the stimuli in both location and pitch tasks were identical and the only difference between the tasks was the instruction to attend to a given stimulus attribute. One of the task-related findings in Study III was an amplitude difference between the N1m elicited in the match condition of the location and pitch tasks. Most likely, the higher N1m amplitude in the location task reflects dissociation between audiospatial and frequency information processing induced by selective attention to the location or pitch of the stimuli. In both tasks, the N1m amplitude was higher in the memory than in the match and non-match conditions. In the pitch task, the N1m amplitude was lowest in the match condition. This distribution of amplitudes across experimental conditions may be explained by a decrease of the amplitude in response to the repeated stimulus. However, in the location task the smallest amplitude of the N1m was observed in the non-match condition. No task-related differences in the electric and magnetic

N1 components were observed during the memory condition. The retention of the cue stimulus and the tuning of attention to its attribute (location or pitch) during the delay period may have induced the task-related differences between the ERPs elicited by the second, target stimulus. Thus, selective attention, which has been shown to modulate the amplitude of N1 and N1m components of auditory ERPs (Picton and Hillyard, 1974; Rif et al., 1991; Näätänen and Alho, 1995; Woldorff, 1995), may have contributed to the present findings. However, the effects of attention on the spatial and nonspatial stimulus features may differ from each other. In recent PET studies, spatially directed attention to auditory stimulation was shown to enhance activity in auditory cortical areas of the hemisphere contralateral to the attended ear (Alho et al., 1999) and to decrease activation in the ipsilateral hemisphere (O'Leary et al., 1996). Enhanced activation may indicate facilitated processing of auditory information in this hemisphere. In the match condition of the location task, the target stimulus always occurred in the same location as the cue. The retention of the cue location during the delay period may have enhanced activation in the hemisphere contralateral to the attended location, resulting in facilitation of processing in this hemisphere. This may explain the increase in the amplitude of the N1m component in the match condition of the location task compared with the corresponding components elicited in the pitch task. Although the task-related difference in the amplitude of the electric N1 component was not significant in any of the experimental conditions, the amplitude of the N1 tended to be higher in the match condition of the location than pitch task. Thus, the match condition appears to be more sensitive than the non-match condition to task-related differences.

Another indication of a functional dissociation between spatial and nonspatial information processing was the shorter N1 latency in the match condition of the location task than in the same condition of the pitch task. The results of mismatch negativity (MMN) studies (Schröger 1995; Schröger and Wolff, 1997) have demonstrated faster preattentive processing of location relative to frequency information, which was indicated by a shorter latency of the MMN generated by automatic detection of sound location changes as compared with detection of frequency changes. Thus the faster automatic encoding of spatial than nonspatial information may underlie the facilitation of the working memory processing of auditory location.

Analysis of the behavioral data revealed significant differences between the reaction times (RTs) in the location and pitch tasks. However, the type of task did not affect the number of incorrect responses or the subjective difficulty level. In several studies RTs, the number of incorrect responses, and the subjective difficulty evaluation score have been shown to increase with increasing memory load (Carlson et al., 1998; Vuontela et al., 1999; Martinkauppi et al., 2000). In Study III, memory load was the same in both tasks, the level of subjective difficulty almost equal, and both tasks were performed at a similarly high level of accuracy (94–98%). However, an increase in RTs with memory load is not always coupled with a decrease in task performance accuracy (Rypma et al., 1999). Thus, longer RTs during pitch task performance may, on one hand, indicate higher cognitive demands of this task. On

the other hand, it is also possible that the difference in the RTs reflects some functional differences in the working memory processing of domain-specific information.

In addition to the functional dissociation, the results of Study II also suggest subareal segregation of spatial and nonspatial auditory processing. In the right hemisphere in all subjects, the source of the N1m elicited during the location task was situated medially to the source of the N1m elicited during the pitch task. However, one should keep in mind that apparent differences in the source location may result from differences in the relative amplitudes of multiple sources.

Electrophysiological single cell recordings and anatomical tracing studies in nonhuman primates indicate that the caudo-medial part of the auditory cortex is located medially to the primary auditory AI area (Kaas et al., 1999; Romanski et al., 1999; Recanzone et al., 2000). The caudo-medial field has been suggested to take part in audio-spatial processing (Rauschecker et al., 1997) and to include proportionally more neurons sensitive to sound location than the auditory core areas (Recanzone et al., 2000). Although it is not known whether the human auditory cortex contains areas homologous with the monkey auditory fields, it is plausible that some basic features of cortical processing are similar in the two species. The finding of Study III indicating different locations of the sources of the N1m components induced by the location and pitch tasks is in line with the results of the above-mentioned studies suggesting at least partial structural segregation of spatial and nonspatial information processing in the auditory cortex.

Analysis of the source locations of the N1m also demonstrated a prominent hemispheric difference along the *y-axis*. In the right hemisphere, the N1m generators of all experimental conditions were located significantly anterior to the generators of the corresponding N1m components in the left hemisphere. This finding, which was also obtained in Study IV, is in line with the results of some previous studies (Pantev et al., 1998; Teale et al., 1998; Tiihonen et al., 1998; Tiitinen et al., 1999) and may reflect the anatomical hemispheric asymmetry of the Heschl's gyrus and the planum temporale (Rojas et al., 1997; Westbury et al., 1999) in healthy right-handed subjects.

In conclusion, the results of Study III provide evidence for at least partial dissociation of spatial and nonspatial auditory processing, which is reflected as differences in the amplitude, latency and source location of the electric and magnetic N1 components elicited during location and pitch working memory task performance.

6.3.2. The N1 component in the 3-back/DMTS task (Study IV)

Considering the results of Studies I-III, it is possible to suggest that at least the early stages of working memory processing of spatial and non-spatial auditory information are partially segregated in the functional neuronal networks, and that this segregation might be memory load-dependent. In order to test this suggestion, a novel behavioral paradigm was designed. This paradigm enables variation of memory load in a parametric manner and separation of “memory cue” and “probe” conditions. Thus it is possible to record memory-related responses that are not biased by a preparatory motor component.

Analysis of the behavioral data did not show any significant differences between the location and pitch task performance. This result indicates that the tasks used in Study IV were well balanced, and the auditory ERPs obtained during location and pitch task performance were valid for further analysis of task-related differences.

The type of task significantly affected the latency and source location of the magnetic but not the electric counterpart of the N1 component. The latency of the N1m was shorter during location than pitch task performance. This finding is generally in line with the results of Study III employing location and pitch delayed matching-to-sample tasks. However, in Study III the task-related latency difference of the N1 was found in the match but not memory condition, whereas in Study IV it was observed in the cue III condition. This dissimilarity in the results may be due to differences in the design of the two studies. In the Study IV, the requirement to retain the order of the consecutive cues may have enhanced selective attention to the task-relevant attribute and explain task-related differences observed in the “cue” epochs.

A task-related difference was also found in the location of the N1m generator in the Cue epochs. The sources of the N1m components recorded during the pitch task were located significantly superiorly to the N1m sources in the location task, which suggests subareal segregation. Although the difference was rather small, it was consistent across conditions and subjects.

6.3.3. Effect of memory load on task-related differences (Study IV)

In Study IV, task-related differences were also found in the later components of auditory ERPs. The amplitude of the N2 component was significantly more negative in the pitch than location task. The N2 component has been shown to be modality specific and affected by the stimulus class within the same modality. Its scalp distribution was significantly different in visual discrimination tasks involving either semantic or physical features of the stimuli (Ritter et al., 1983), and its amplitude in a divided attention task was modulated by alterations in the attended attribute (Omoto et al., 2001). In the latter study, the N2 component was enhanced by alterations in the color but not the location of the stimulus, in other words, in the nonspatial but not the spatial factor.

A task-related difference was also observed in a deflection at the latency of about 400 ms and was most prominent at the central and centro-parietal sites. This deflection, separating the P3 component from the positive slow wave, was more negative during the pitch than the location task. In a recent study, Alain and colleagues (2001) reported an amplitude difference between auditory ERPs recorded during spatial and nonspatial matching-to-sample tasks at a similar time interval (between 300 and 500 ms). In line with the finding from Study IV, the mean ERP amplitude recorded at the centro-parietal sites during the pitch task was more negative than the corresponding amplitude observed during the location task. In addition, the authors reported a task-related difference with a reversed polarity within the same time window at the fronto-temporal regions, which was not observed in Study IV. The discrepancy

between these two studies may be due to differences in the design and data collection (e.g., the reference site).

In the study by Chao et al. (1995) employing an auditory recognition task, an N4 component was registered to the presentation of an environmental sound and to the repetition of the stimulus after a long delay (over 4 seconds) but not after a short, 2-second delay. This finding led the authors to suggest that at long delays the neocortical processing may not be sufficient for stimulus recognition and additional memory search mechanisms are engaged. Results from intracranial recordings concerning the N4 component (e.g., Smith et al., 1986) suggest the involvement of medial temporal lobe circuits in the mechanisms related to memory search and encoding of complex stimuli. Considering the requirements of the current task to retain the memory cue for 6 seconds as well as the order of consecutive cues, the negative-going deflection at the latency around 400 ms in Study IV most probably reflects the encoding into working memory the complex memorandum consisting of single items. This process may engage partially separate neuronal networks, depending on the relevant stimulus attribute, resulting in the task-related amplitude difference around 400 ms.

The next prominent task-related amplitude difference was observed in the PSW at a time window of 450-650 ms. The amplitude of the PSW was higher in the location than pitch task suggesting a stronger involvement of the parietal areas in spatial than nonspatial auditory information processing. A significant task-related difference was found only in cue I condition. This finding is in line with the results of Study I, in which 1-back but not 2-back auditory task performance was selectively disrupted by the distractors qualitatively similar to the memoranda, and supports the hypothesis of load-dependent dissociation between spatial and nonspatial information processing (Study I, Vuontela et al., 1999).

In conclusion, task-related differences were found in the N1, N2, in the deflection at the latency of about 400 ms and in PSW recorded during spatial and nonspatial working memory tasks, but not in the Late Slow Waves. These findings suggest that separate neuronal networks are involved in the perceptual processing and encoding into working memory of spatial and nonspatial auditory information, whereas the maintenance of this information is mainly accomplished by a common, nonspecific neuronal network.

6.3.4. Effect of task on cortical generators of the P3 and PSW in the responses to probes (Study V)

Study V focused on evoked responses to the probe stimuli from the same experimental setup and recordings that were described in Study IV. Several associative temporal and parietal cortical areas contributed to the generation of the slow evoked responses. Within the temporal lobe, activity was seen bilaterally around the posterior (here called the occipito-temporal source) and the central parts of the STS (the temporal source), with right-hemispheric dominance for the temporal source. No activity was observed in the primary or secondary auditory cortex on the supratemporal plane within the analyzed time interval. In the parietal lobes, activity was found in the precuneus and around the junction of the postcentral and intraparietal sulci (the parietal source), mainly in the left hemisphere.

Activation of the precuneus has been demonstrated in various neuroimaging studies employing auditory or visual working memory tasks (Martinkauppi et al., 2000; Maeder et al., 2001; Zurowski et al., 2002), tasks requiring selective attention shifts (Nagahama et al., 1999) or mental calculations (Zago and Tzourio-Mazoyer, 2002), suggesting that this structure is part of a supramodal neural network engaged in such processes as allocation of attention, retrieval of information and updating of working memory buffer.

The predominantly left-hemispheric activity that was detected within the parietal source is consistent with a recent fMRI study by Lewis and colleagues (2004) in which subjects performed a multiple-choice motor response task with the right hand during sound recognition. Activation in an area close to the left parietal source was also observed in another fMRI study (Culham et al., 2003) during precise grasping with the right hand. Thus the left-sided activation of the parietal source in Study V may reflect preparatory activity related to motor responses of the right hand.

One of the two main findings of Study V concerns the differences between the P3 and PSW. This study revealed functional differences between the networks involved in the generation of the P3 and PSW. The activity within the temporal lobes during slow evoked responses increased with time in the postero-anterior direction: the occipito-temporal source was most active during the generation of the P3 component whereas activity in the temporal source increased over time and reached its maximum during the PSW generation.

The role of the posterior temporal areas in the generation of the P3 was emphasized in a combined electrophysiological and single photon emission tomography study by Ebmeier et al. (1995). The activation in the posterior temporal regions (an area close to the occipito-temporal source in Study V) was shown to correlate positively with the amplitude of the P3 component in an auditory target-detection task. In Study V, the amplitude of the temporal source was higher in the right than left hemisphere. In line with this finding, an interhemispheric asymmetry in the temporal activity was described in an MEG study by Raji et al. (1997), where omitted auditory stimuli elicited responses in the STS more often in the right than left hemisphere, suggesting that the right temporal area is a possible generator of slow evoked responses.

The P3 and PSW recorded in Study V differed from each other with respect to match and non-match trials: the electrical P3 had its amplitude maximum in the match and the PSW in the non-match condition. This finding is in agreement with an earlier study employing the Sternberg paradigm (Pelosi et al., 1998) in which the amplitude of the P3 in the auditory task was higher for positive than negative probes, while the amplitude of the PSW elicited in the same task was higher for negative probes. The activity in the precuneus was affected by the Probe type and Component interaction: in the non-match condition, in line with the ERP data, the amplitude of the evoked field increased during transition from the P3 to PSW increased during transition from the P3 to the PSW. Furthermore, the electric P3 and PSW were differently related to the behavioral data: the latency of the PSW but not that of the P3 was shown to correlate positively with RTs. Taken together, results of Study V suggest that the P3 and PSW represent different neural events. The P3 elicited in the responses to probes during

working memory task may reflect, in addition to other functions, the matching of the probe with the memory trace of the previously presented cue. The increase of the PSW amplitude in the non-match condition may be related to the engagement of additional retrieval mechanisms in order to ensure that the decision "different" was correct.

Another important result obtained in Study V concerns the differences between spatial and nonspatial working memory processing in the auditory system: the occipito-temporal generator of the P3 was activated more strongly during the performance of the location task while the activity of the left temporal generator of the PSW was enhanced during working memory processing of sound pitch, although the latter result was not statistically quite significant ($p = 0.067$). In the fMRI study by Lewis et al. (2004) the posterior portions of the middle temporal gyri (pMTG), close to the occipito-temporal area described in Study V, were shown to be activated bilaterally during recognition of environmental sounds produced by manipulated objects and objects that typically have strong visual motion associations. Since the activated pMTG areas in that study partially overlapped the cortical areas involved in high-level processing of visual motion, the pMTG foci were suggested to process multimodal or supramodal information about object-associated motion. Another fMRI study by Warren and colleagues (2002) provided evidence of the involvement of the parieto-occipital junction in the processing of sound motion.

Results of the above-mentioned studies and the present finding that activation in the occipito-temporal source is stronger during location than pitch task performance indicate that processing of auditory spatial information recruits the posterior temporo-parietal pathway. Results of Study V also suggest that auditory non-spatial information might be processed in more anterior temporal areas, which would be consistent with the result of an fMRI study where the right anterior STS region was shown to be selectively activated by auditory object feature variation contrasted to variation in stimulus location (Zatorre et al., 2004). Results of Studies III and IV suggest that the segregation of auditory information processing to "what" and "where" functional networks takes place already at about 100 ms from the stimulus onset within the auditory cortex on the supratemporal plane. Study V extends this finding by demonstrating that segregation also takes place at the time intervals of slow evoked responses in the occipito-temporal and possibly middle temporal cortical areas.

Thus, electrophysiological techniques with excellent time resolution and relatively good localization ability enable to address not only the issue of dissociation between "what" and "where" information processing in the auditory system but also the question where and when the possible dissociation takes place in the human brain.

7. GENERAL CONCLUSIONS

The present Ph.D. project aimed to test the hypothesis that processing of spatial and nonspatial auditory information is segregated in the human brain. On the basis of the results the following conclusions can be drawn:

1. Spatial and nonspatial auditory information processing is partially segregated (studies I, III, IV and V).
2. Task-related (spatial vs. nonspatial) differences were dependent on memory load. They were observed only at a moderate memory load (Studies I and IV), suggesting that the segregation depends also on factors other than the nature of the auditory information, such as mnemonic demands.
3. Electrophysiological techniques enabled detection of the spatio-temporal dynamics of differences between spatial and nonspatial auditory processing. Differences were primarily observed during the generation of the N1 component within the auditory cortex on the supratemporal plane (studies III and IV). At the time range of the slow evoked responses (the P3 and PSW) the differences occurred in associative occipito-temporal and temporal areas (study V).
4. Late slow waves were affected by memory load but not the type of task (studies II and IV).

These results suggest that separate neuronal networks are involved in the attribute-specific analysis of auditory stimuli and their encoding into working memory, whereas the maintenance of spatial and nonspatial auditory information is accomplished by a common, nonspecific neuronal network.

ACKNOWLEDGMENTS

This work was carried out in the Neuroscience Unit, Institute of Biomedicine, Department of Physiology and BioMag Laboratory, Helsinki University Central Hospital. I wish to thank the former and present heads of the department of Physiology, Professors Olli Jänne, Dag Stenberg and Antti Pertovaara, and the directors of BioMag Laboratory, Dr. Risto Ilmoniemi and Dr. Juha Montonen, for giving me the opportunity to conduct my research work in the excellent facilities. The studies were financially supported by the Center for International Mobility (CIMO), The Academy of Finland and Helsinki University Central Hospital research funds.

For most I wish to address my deepest gratitude to my supervisor, Docent Synnöve Carlson, who professionally guided my research work, inspired me with her enthusiasm and optimism and lead me towards a mature and independent specialist. During these years she has been not only a supervisor but one of the dearest friends of our family.

I also wish to thank my first teacher, Professor Anatoly Vasiliev who supervised my masters training since the first year of specialization. I still remember and carefully follow the “golden rules” of experimental research: “Change only one condition at a time!” and “Never give up!” My warmest gratitude to my university teachers: Alexander Batuev, Gennady Kulikov, Alexander Alexandrov, Nadezhda Andreeva, Ljudmila Stankevich and Ekaterina Vinogradova who with their professional lectures opened the world of Neuroscience to me.

I wish to acknowledge and thank the reviewers of my thesis, Professor Heikki Hämäläinen and Docent Jari Karhu, for their constructive and valuable comments. My deepest gratitude is due to Docent Jyrki Mäkelä for agreeing to act as my opponent at the public defense of this dissertation. I would also like to thank warmly Marja-Liisa Tiainen, the secretary of the Department of Physiology for her excellent help in all practical matters.

I would like to express my warmest gratitude to Docent Ilkka Linnankoski for his friendly support and care which made our adaptation in Finland easier.

I am deeply grateful to my coauthors Kimmo Alho, Antti Korvenoja, Pia Rämä and Hannu Aronen for their valuable contribution and the creative discussions. Special thanks to Elina Pihko and Yoshio Okada for their guidance and support, and to Suvi Hekkilä for excellent technical assistance in BioMag Laboratory. My special gratitude is due to my friend and colleague Vadim Nikulin, who patiently guided my very first diffident steps in magnetoencephalography.

I also wish to thank all present and former members of our unit: Ernst Mekke, Virve Vuontela, Johanne Pallesen, Shelley Ylioja, Maartje van Kregten, Liisa Peltonen, Katrina Lauren, Wei Hong, Tuomas Nevenon and Dmitrij Tichonravov for creating a nice working atmosphere and the sense of a team.

My sincere thanks to my friends, Elena Kushnerenko and Ivan Pavlov, Elena Lobytseva and Vladimir Aseyev, Anna Shestakova and Vasilij Kljucharev, Anna Popsueva and Aleksej Veselov, Olga Varjagina, Anna Kalinchuk, Andrej Kostin, Nikolai Novitski and Victor Vorobjev who have always been close to my family and shared my ups and downs during my stay in Finland.

And finally, I wish to express my warmest gratitude to my family. I thank my parents and brother for their infinite love and support. My special gratitude is due to my husband, the best friend and colleague, Denis Artchakov, for his patience, understanding and love. And, of course, my dear daughter Natalia, who is bringing light, happiness and inspiration into my life.

REFERENCES

- Ahissar M, Ahissar E, Bergman H and Vaadia E (1992). Encoding of sound-source location and movement: activity of single neurons and interactions between adjacent neurons in the monkey auditory cortex. *J Neurophysiol* 67: 203-215.
- Ahveninen J, Kähkönen S, Pennanen S, Leisivuori J, Ilmoniemi RJ and Jääskeläinen IP (2002). Tryptophan depletion effects on EEG and MEG responses suggests serotonergic modulation of auditory involuntary attention in humans. *NeuroImage* 16: 1052-1061.
- Alain C, Arnott SR, Hevenor S, Graham S and Grady CL (2001). "What" and "where" in the human auditory system. *Proc Natl Acad Sci USA* 98: 12301-12306.
- Albert ML, Sparks R, von Stockert T and Sax D (1972). A case study of auditory agnosia: linguistic and non-linguistic processing. *Cortex* 8: 427-443.
- Alcaini M, Giard MH, Thevenet M and Pernier J (1994). Two separate frontal components in the N1 wave of the human auditory evoked response. *Psychophysiology* 31: 611-615.
- Alho K, Lavikainen J, Reinikainen K, Sams M and Näätänen R (1990). Event-related brain potentials in selective listening to frequent and rare stimuli. *Psychophysiology* 27: 73-86.
- Alho K, Medvedev SV, Pakhomov SV, Roudas MS, Tervaniemi M, Reinikainen K, Zeffiro T and Näätänen R (1999). Selective tuning of the left and right auditory cortices during spatially directed attention. *Cogn Brain Res* 7: 335-341.
- Altman JA and Vaitulevich SF (1992). [Human auditory evoked potentials and sound source localization] [Russian], Saint-Petersburg: Nauka.
- Altman JA, Rosenblum AS and Lvova VG (1987). Lateralization of a moving auditory image in patients with focal damage of the brain hemisphere. *Neuropsychologia* 25: 435-442.
- Altman JA (1990). Spatial hearing. In: *Auditory system* (Altman JA, Ed.), Leningrad: Nauka, pp 366-448.
- Anderer P, Saletu B, Saletu-Zyhlarz G, Gruber D, Metka M, Huber J and Pascual-Marqui RD (2004). Brain regions activated during an auditory discrimination task in insomniac postmenopausal patients before and after hormone replacement therapy: low-resolution brain electromagnetic tomography applied to event-related potentials. *Neuropsychobiology* 49: 134-153.
- Andersen RA, Roth GL, Aitkin LM and Merzenich MM (1980). The efferent projections of the central nucleus and the pericentral nucleus of the inferior colliculus in the cat. *J Comp Neurol* 194: 649-662.
- Andreassi JL (1995). *Psychophysiology: human behaviour and physiological response*, 3rd ed. Hillsdale, NJ: Lawrence Erlbaum.
- Andreeva NG and Vasil'ev AG (1977). [Responses of neurons of the supraolivary complex to amplitude-modulated signals] [Russian]. *Fiziol Zh SSSR Im IM Sechenova* 63: 469-503.
- Andreeva NG, Obuhov DK, Demjanenko GP and Kamenskaja BG (1985). [Morphology of nervous system] [Russian], Leningrad: Leningrad University Press.
- Anourova I, Rama P, Alho K, Koivusalo S, Kahnari J and Carlson S (1999). Selective interference reveals dissociation between auditory memory for location and pitch. *NeuroReport* 10: 3543-3547.
- Anourova I, Nikouline VV, Ilmoniemi RJ, Hotta J, Aronen HJ and Carlson S (2001). Evidence for dissociation of spatial and nonspatial auditory information processing. *NeuroImage* 14: 1268-1277.
- Antinoro F and Skinner PH (1968). The effects of frequency on the auditory evoked response *J Aud Res* 8: 119-123.
- Anurova I, Artchakov D, Korvenoja A, Ilmoniemi RJ, Aronen HJ and Carlson S (2003). Differences between auditory evoked responses recorded during spatial and nonspatial working memory tasks. *NeuroImage* 20: 1181-1192.
- Arlinger S, Elberling C, Bak C, Kofoed B, Lebech J and Saermark K (1982). Cortical magnetic fields evoked by frequency glides of a continuous tone. *Electroencephalogr Clin Neurophysiol* 54: 642-653.
- Arnott SR, Binns MA, Grady CL and Alain C (2004). Assessing the auditory dual-pathway model in humans. *NeuroImage* 22: 401-408.
- Barcelo F, Martin-Loeches M and Rubia FJ (1997). Event-related potentials during memorization of spatial locations in the auditory and visual modalities. *Electroencephalogr Clin Neurophysiol* 103: 257-267.
- Baru AV (1978). [Auditory structures and sound recognition] [Russian], Leningrad: Nauka.

- Baumgart F, Gaschler-Markefski B, Woldorff MG, Heinze HJ and Scheich H (1999). A movement-sensitive area in auditory cortex. *Nature* 400: 724-726.
- Beagley HA and Knight JJ (1967). Changes in auditory evoked response with intensity. *J Laryngol Otol* 81: 861-873.
- Bear MF, Connors BW and Paradiso MA (2001). The auditory and vestibular systems. In: *Neuroscience Exploring the brain*, 2nd ed. (Katz S, Ed.), Baltimore: Lippincott Williams and Wilkins, pp 349-395.
- Belin P and Zatorre RJ (2000). 'What', 'where' and 'how' in the auditory cortex. *Nature Neurosci* 3: 965-966.
- Belin P, McAdams S, Smith B, Savel S, Thivard L, Samson S and Samson Y (1998). The functional anatomy of sound intensity discrimination. *J Neurosci* 18: 6388-6394.
- Belin P, McAdams S, Thivard L, Smith B, Savel S, Zilbovicius M, Samson S and Samson Y (2002). The neuroanatomical substrate of sound duration discrimination. *Neuropsychologia* 40: 1956-1964.
- Benedict RH, Lockwood AH, Shucard JL, Shucard DW, Wack D and Murphy BW (1998). Functional neuroimaging of attention in the auditory modality. *NeuroReport* 9: 121-126.
- Bilecen D, Scheffler K, Schmid N, Tschopp K and Seelig J (1998). Tonotopic organization of the human auditory cortex as detected by BOLD-fMRI. *Hear Res* 126: 19-27.
- Bilecen D, Seifritz E, Scheffler K, Henning J and Schulte AC (2002). Amplitude of the human auditory cortex: an fMRI study. *NeuroImage* 17: 710-708.
- Binder JR, Liebenthal E, Possing ET, Medler DA and Ward BD (2004). Neural correlates of sensory and decision processes in auditory object identification. *Nat Neurosci* 7: 295-301.
- Bosch V, Mecklinger A and Friederici AD (2001). Slow cortical potentials during retention of object, spatial, and verbal information. *Brain Res Cogn Brain Res* 10: 219-237.
- Bourbon WT, Will KW, Gary HE Jr and Papanicolaou AC (1987). Habituation of auditory event-related potentials: a comparison of self-initiated and automated stimulus trains. *Electroencephalogr Clin Neurophysiol* 66: 160-166.
- Braver TS, Cohen JD, Nystrom LE, Jonides J, Smith EE and Noll DC (1997). A parametric study of prefrontal cortex involvement in human working memory. *NeuroImage* 5: 49-62.
- Brechmann A, Baumgart F and Scheich H (2002). Sound-level-dependent representation of frequency modulations in human auditory cortex: a low-noise fMRI study. *J Neurophysiol* 87: 423-433.
- Bremmer F, Schlack A, Shah NJ, Zafiris O, Kubischik M, Hoffmann K, Zilles K and Fink GR (2001). Polymodal motion processing in posterior parietal and premotor cortex: a human fMRI study strongly implies equivalencies between humans and monkeys. *Neuron* 29: 287-296.
- Brugge JF, Reale RA, Hind JE, Chan JCK, Musicant AD and Poon PWF (1994). Simulation of free-field sound sources and its application to studies of cortical mechanisms of sound localization in the cat. *Hear Res* 73: 67-84.
- Brugge JF, Reale RA and Hind JE (1996). The structure of spatial receptive fields of neurons in primary auditory cortex of the cat. *J Neurosci* 16: 4420-4437.
- Buchsbaum M (1976). Self-regulation of stimulus intensity. Augmenting/reducing and the average evoked response. In: *Consciousness and self-regulation* (Schwartz GE and Shapiro D, Eds.), New York: Plenum, pp 101-135.
- Budd TW, Barry RJ, Gordon E, Rennie C and Michie PT (1998). Decrement of the N1 auditory event-related potential with stimulus repetition: habituation vs. refractoriness. *Int J Psychophysiology* 31: 51-68.
- Burle B, Vidal F and Bonnet M (2004). Electroencephalographic nogo potentials in a no-movement context: the case of motor imagery in humans. *Neurosci Lett* 360: 77-80.
- Bushara KO, Weeks RA, Ishii K, Catalan M-J, Tian B, Rauschecker JP and Hallett M (1999). Modality-specific frontal and parietal areas for auditory and visual spatial localization in humans. *Nature Neurosci* 2: 759-766.
- Butler RA (1968). Effect of changes in stimulus frequency and intensity on habituation of the human vertex potential. *J Acoust Soc Am* 44: 945-950.
- Butler RA (1972). Frequency specificity of the auditory evoked response to simultaneously and successively presented stimuli. *Electroencephalogr Clin Neurophysiol* 33: 277-282.
- Calford MB and Aitkin LM (1983). Ascending projections to the medial geniculate body of the cat: evidence for multiple, parallel auditory pathways through thalamus. *J Neurosci* 3: 2365-2380.

- Carlson S, Martinkauppi S, Rämä P, Salli E, Korvenoja A and Aronen HJ (1998) Distribution of cortical activation during visuospatial n-back tasks as revealed by functional magnetic resonance imaging. *Cereb Cortex* 8: 743-752.
- Celesia GG, Broughton RJ, Rasmussen T and Branch C (1968). Auditory evoked responses from the exposed human cortex. *Electroencephalogr Clin Neurophysiol* 24: 458-466.
- Celesia GG (1976). Organization of auditory cortical areas in man. *Brain* 99: 403-414.
- Ceponiene R, Rinne T and Näätänen R (2002). Maturation of cortical sound processing as indexed by event-related potentials. *Clin Neurophysiol* 113: 870-882.
- Chao LL, Nielsen-Bohlman L and Knight RT (1995). Auditory event-related potentials dissociate early and late memory processes. *Electroencephalogr Clin Neurophysiol* 96: 157-168.
- Clarke S, Adriani M and Bellmann A (1998). Distinct short-term memory systems for sound content and sound localization. *NeuroReport* 9: 3433-3437.
- Clarke S, Bellmann A, Meuli RA, Assal G and Steck AJ (2000). Auditory agnosia and auditory spatial deficits following left hemispheric lesions: evidence for distinct processing pathways. *Neuropsychologia* 38: 797-807.
- Clarke S, Bellmann Thiran A, Maeder P, Adriani M, Vernet O, Regli L, Cuisenaire O and Thiran JP (2002). What and where in human audition: selective deficits following focal hemispheric lesions. *Exp Brain Res* 147: 8-15.
- Cohen YE and Wessinger CM (1999). Who goes there? *Neuron* 24: 769-771.
- Courtney SM, Ungerleider LG, Keil K and Haxby JV (1996). Object and spatial visual working memory activate separate neural systems in human cortex. *Cereb Cortex* 6: 39-49.
- Culham JC, Danckert SL, DeSouza JF, Gati JS, Menon RS and Goodale MA (2003). Visually guided grasping produces fMRI activation in dorsal but not ventral stream brain areas. *Exp Brain Res* 153: 180-189.
- Daruna JH, Nelson AV and Green JB (1989). Unilateral temporal lobe lesions alter P300 scalp topography. *Int J Neurosci* 46: 243-247.
- Davis PA (1939). Effects of acoustic stimuli on the waking human brain. *J Neurophysiol* 2: 494-499.
- Davis H and Zerlin S (1966). Acoustic relations of the human vertex potential. *J Acoust Soc Am* 39: 109-116.
- Desmedt JE (1980). P300 in serial tasks: an essential post-decision closure mechanism. *Prog Brain Res* 54: 682-686.
- Deutsch D (1970). Tones and numbers: specificity of interference in immediate memory. *Science* 168: 1604-1605.
- Donchin E and Coles MGH (1988). Precommentary: is the P3 component a manifestation of context updating? *Behav Brain Sci* 11: 355-425.
- Donchin E, Ritter W and McCallum WC (1978). Cognitive psychophysiology: The endogenous components of the ERP. In: *Event-related brain potentials in man* (Callaway E, Tueting P and Koslow SH, Eds.), New York: Academic Press, pp 349-441.
- Duncan-Johnson CC and Donchin E (1977). On quantifying surprise: The variation of event-related potentials with subjective probability. *Psychophysiology* 14: 456-467.
- Duncan-Johnson CC and Donchin E (1982). The P300 component of the event-related brain potential as an index of information processing. *Biol Psychol* 14: 1-52.
- Ebmeier KP, Steele JD, MacKenzie DM, O'Carroll RE, Kydd RR, Glabus MF, Blackwood DH, Rugg MD and Goodwin GM (1995). Cognitive brain potentials and regional cerebral blood flow equivalents during two- and three-sound auditory "oddball tasks". *Electroencephalogr Clin Neurophysiol* 95: 434-443.
- Eimer M (1993). Effects of attention and stimulus probability on ERPs in a go/nogo task. *Biol Psychol* 35: 123-138.
- Eisenman LM (1974). Neural encoding of sound location: an electrophysiological study in auditory cortex (AI) of the cat using free field stimuli. *Brain Res* 75: 203-214.
- Elberling C, Bak C, Kofoed B, Lebech J and Saermark K (1982). Auditory magnetic fields: source location and 'tonotopical organization' in the right hemisphere of the human brain. *Scand Audiol* 11: 61-65.
- Elbert T, Rockstroh B, Hampson S, Pantev C and Hoke M (1994). The magnetic counterpart of the contingent negative variation. *Electroencephalogr Clin Neurophysiol* 92: 262-272.

- Engelien A, Silbersweig D, Stern E, Huber W, Doring W, Frith C and Frackowiak RS (1995). The functional anatomy of recovery from auditory agnosia. A PET study of sound categorization in a neurological patient and normal controls. *Brain* 118: 1395-1409.
- Enoki H, Sanada S, Yoshinaga H, Oka E and Ohtahara S (1993). The effect of age on the N200 component of the auditory event-related potentials. *Cogn Brain Res* 1: 161-167.
- Ervin FR and Mark VH (1964). Studies of the human thalamus IV: Evoked response. *Ann New York Acad Science* 112: 81-92.
- Fabiani M, Gratton G, Karis D and Donchin E (1987). The definition, identification and reliability of measurement of the P3 component of the event-related brain potential. In: *Advances in Psychophysiology*, vol. 2 (Ackles PK, Jennings JR, Coles MG, Eds.), Greenwich, CT: JAI Press, pp 1-78.
- Falkenstein M, Hohnsbein J, Hoormann J and Blanke L (1991). Effects of crossmodal divided attention on late ERP components II Error processing in choice reaction tasks. *Electroencephalogr Clin Neurophysiol* 78:447-455.
- Falkenstein M, Koshlykova NA, Kiroj VN, Hoormann J and Hohnsbein J (1995). Late ERP components in visual and auditory Go/Nogo tasks. *Electroencephalogr Clin Neurophysiol* 96: 36-43.
- Falkenstein M, Hoormann J and Hohnsbein J (1999). ERP components in Go/Nogo tasks and their relation to inhibition *Acta Psychol (Amst)* 101: 267-291.
- Fitzgerald PG and Picton TW (1983). Event-related potentials recorded during the discrimination of improbable stimuli. *Biol Psychol* 17: 241-276.
- Fitzpatrick DC, Batra R, Stanford TR and Kuwada S (1997). A neuronal population code for sound localization. *Nature* 388: 871-874.
- Friedman D, Cycowicz YM, Gaeta H (2001). The novelty P3: an event-related brain potential (ERP) sign of the brain's evaluation of novelty. *Neurosci Biobehav Reviews* 25: 355-373.
- Friedman D and Simpson G (1994). Amplitude and scalp distribution of target and novel events: effects of temporal order in young, middle-aged and older adults. *Cogn Brain Res* 2: 49-63.
- Frodl-Bauch T, Gallinat J, Meisenzahl EM, Moller HJ and Hegerl U (1999). P300 subcomponents reflect different aspects of psychopathology in schizophrenia. *Biol Psychiatry* 45: 116-126.
- Fruhstorfer H, Soveri P and Jarvilehto T (1970). Short-term habituation of the auditory evoked response in man. *Electroencephalogr Clin Neurophysiol* 28: 153-161.
- Fruhstorfer H (1971). Habituation and dishabituation of the human vertex response. *Electroencephalogr Clin Neurophysiol* 30: 306-312.
- Fujioka T, Kakigi R, Gunji A and Takeshima Y (2002). The auditory evoked magnetic fields to very high frequency tones. *Neuroscience* 112: 367-381.
- Furukawa S and Middlebrooks JC (2001). Sensitivity of auditory cortical neurons to locations of signals and competing noise sources. *J Neurophysiol* 86: 226-240.
- Furukawa S and Middlebrooks JC (2002). Cortical representation of auditory space: information-bearing features of spike patterns. *J Neurophysiol* 87: 1749-1762.
- Furukawa S, Xu L and Middlebrooks JC (2000). Coding of sound-source location by ensembles of cortical neurons. *J Neurosci* 20: 1216-1228.
- Galaburda A and Sanides F (1980). Cytoarchitectonic organization of the human auditory cortex. *J Comp Neurol* 190: 597-610.
- Garcia-Larrea L and Cezanne-Bert G (1998). P3, positive slow wave and working memory load: a study on the functional correlates of slow wave activity. *Electroencephalogr Clin Neurophysiol* 108: 260-273.
- Gazzaniga MS, Glass AV, Sarno MT and Posner JB (1973). Pure word deafness and hemispheric dynamics: a case history. *Cortex* 9: 136-143.
- Geffen G, Wright M, Green H, Gillespie N, Smyth DC, Evans D and Geffen L (1997). Effects of memory load and distraction on performance and event-related slow potentials in a visuospatial working memory task. *J Cogn Neurosci* 9: 743-757.
- George JS, Aine CJ, Mosher JC, Schmidt DM, Ranken DM, Schlitt HA, Wood CC, Lewine JD, Sanders JA and Belliveau JW (1995). Mapping function in the human brain with magnetoencephalography, anatomical magnetic resonance imaging, and functional magnetic resonance imaging. *J Clin Neurophysiol* 12: 406-431.
- Giard MH, Perrin F, Echallier JF, Thevenet M, Froment JC and Pernier J (1994). Dissociation of temporal and frontal components in the human auditory N1 wave: a scalp current density and dipole model analysis. *Electroencephalogr Clin Neurophysiol* 92: 238-252.

- Giraud AL, Lorenzi C, Ashburner J, Wable J, Johnsrude I, Frackowiak R and Kleinschmidt A (2000). Representation of the temporal envelope of sounds in the human brain. *J Neurophysiol* 84: 1588-1598.
- Goldman-Rakic PS (1994). The issue of memory in the study of prefrontal functions. In: *Motor and cognitive functions of the prefrontal cortex* (Thierry AM, Glowinski J, Goldman-Rakic PS and Christen Y, Eds.), Berlin: Springer, pp. 112-122.
- Goldman-Rakic PS (1995). Architecture of the prefrontal cortex and the central executive. In: *Structure and functions of the human prefrontal cortex* (Ann NY Acad Sci, vol. 769), New York: NY Acad Sci, pp. 71-83.
- Griffiths TD and Green GG (1999). Cortical activation during perception of a rotating wide-field acoustic stimulus. *NeuroImage* 10: 84-90.
- Griffiths TD, Bench CJ and Frackowiak RS (1994). Human cortical areas selectively activated by apparent sound movement. *Curr Biol* 4: 892-895.
- Griffiths TD, Buchel C, Frackowiak RS and Patterson RD (1998a). Analysis of temporal structure in sound by the human brain. *Nat Neurosci* 1: 422-427.
- Griffiths TD, Rees G, Rees A, Green GGR, Witton C, Rowe D, Buchel C, Turner R and Frackowiak RSJ (1998b). Right parietal cortex is involved in the perception of sound movement in humans. *Nature Neurosci* 1: 74-79.
- Griffiths TD, Rees A, Witton C, Shakir RA, Henning GB and Green GGR (1996). Evidence for a sound movement area in the human cerebral cortex. *Nature* 383: 425-427.
- Griffiths TD, Rees A, Witton C, Cross PM, Shakir RA and Green GGR (1997). Spatial and temporal auditory processing deficits following right hemisphere infarction: A psychophysiological study. *Brain* 120: 785-794.
- Griffiths TD, Uppenkamp S, Johnsrude I, Josephs O and Patterson RD (2001). Encoding of the temporal regularity of sound in the human brainstem. *Nat Neurosci* 4: 633-637.
- Grigor'eva TI, Figurina II and Vasil'ev AG (1988). Role of the medial geniculate body in the production of conditioned reflexes to amplitude-modulated stimuli in rats. *Neurosci Behav Physiol* 18: 25-31.
- Grigor'eva TI, Figurina II and Vasil'ev AG (1987). [Role of the geniculate body in performing conditioned reflexes to amplitude-modulated stimuli in the rat][Russian]. *Zh Vyssh Nerv Deiat Im I P Pavlova* 37: 265-271.
- Grigor'eva TI and Vasil'ev AG (1981a). [Role of the inferior colliculi in the formation of conditioned reflexes to amplitude-modulated stimuli in rats][Russian]. *Zh Vyssh Nerv Deiat Im I P Pavlova* 31: 557-563.
- Grigor'eva TI and Vasil'ev AG (1981b). [Role of the auditory cortex in the formation of complex reflexes to amplitude-modulated stimuli in rats][Russian]. *Zh Vyssh Nerv Deiat Im I P Pavlova* 31: 284-291.
- Grippo A, Pelosi L, Mehta V and Blumhardt LD (1996). Working memory in temporal lobe epilepsy: an event-related potential study. *Electroencephalogr Clin Neurophysiol* 99: 200-213.
- Hackett TA, Stepniewska I and Kaas JH (1999). Prefrontal connections of the parabelt auditory cortex in macaque monkeys. *Brain Res* 817: 45-58.
- Halgren E, Baudena P, Clarke JM, Heit G, Liegeois C, Chauvel P and Musolino A (1995a). Intracerebral potentials to rare target and distractor auditory and visual stimuli. I. Superior temporal plane and parietal lobe. *Electroencephalogr Clin Neurophysiol* 94: 191-220.
- Halgren E, Baudena P, Clarke JM, Heit G, Marinkovic K, Devaux B, Vignal JP and Biraben A (1995b). Intracerebral potentials to rare target and distractor auditory and visual stimuli. II. Medial, lateral and posterior temporal lobe. *Electroencephalogr Clin Neurophysiol* 94: 229-250.
- Halgren E, Marinkovic K and Chauvel P (1998). Generators of the late cognitive potentials in auditory and visual oddball tasks. *Electroencephalogr Clin Neurophysiol* 106: 156-164.
- Hall DA, Johnsrude IS, Haggard MP, Palmer AR, Akeroyd MA and Summerfield AQ (2002). Spectral and temporal processing in human auditory cortex. *Cereb Cortex* 12: 140-149.
- Hall DA, Hart HC and Johnsrude IS (2003). Relationships between human auditory cortical structure and function. *Audiol Neurootol* 8: 1-18.
- Hari R and Mäkelä JP (1986). Neuromagnetic responses to frequency modulation of a continuous tone. *Acta Otolaryngol Suppl* 432: 26-32.
- Hari R, Kaila K, Katila T, Tuomisto T and Varpula T (1982). Interstimulus interval dependence of the auditory vertex response and its magnetic counterpart: implications for their neural generation. *Electroencephalogr Clin Neurophysiol* 54: 561-569.
- Hari R, Pelizzzone M, Mäkelä JP, Hallstrom J, Leinonen L and Lounasmaa OV (1987). Neuromagnetic responses of the human auditory cortex to on- and offsets of noise bursts. *Audiology* 26: 31-43.

- Hari R (1990). The neuromagnetic method in the study of the human auditory cortex. In: Auditory evoked magnetic fields and electric potentials. Advances in Audiology, vol. 6 (Grandori F, Hoke M and Romani GL, Eds.), Karger, Basel, pp 222-282.
- Harms MP and Melcher JR (2002). Sound repetition rate in the human auditory pathway: representations in the waveshape and amplitude of fMRI activation. *J Neurophysiol* 88: 1433-1450.
- Harrington DL, Haaland KY and Knight RT (1998). Cortical networks underlying mechanisms of time perception. *J Neurosci* 18: 1085-1095.
- Hart HC, Palmer AR and Hall DA (2002). Heschl's gyrus is more sensitive to tone level than non-primary auditory cortex. *Hear Res* 171: 177-190.
- Hegerl U and Frodl-Bauch T (1997). Dipole source analysis of P300 component of the auditory evoked potential: a methodological advance? *Psychiatry Res* 74: 109-118.
- Heil P and Irvine DR (1998). The posterior field P of cat auditory cortex: coding of envelope transients. *Cereb Cortex* 8(2): 125-141.
- Heil P, Rajan R and Irvine DR (1994). Topographic representation of tone intensity along the isofrequency axis of cat primary auditory cortex. *Hear Res* 76: 188-202.
- Hillyard SA, Hink RF, Schwent VL and Picton TW (1973). Electrical signs of selective attention in the human brain. *Science* 182: 177-180.
- Hillyard SA (1981). Selective auditory attention and early event-related potentials: a rejoinder. *Can J Psychol* 35: 159-174.
- Hirata Y, Kuriki S and Pantev C (1999). Musicians with absolute pitch show distinct neural activities in the auditory cortex. *NeuroReport* Apr 6;10(5): 999-1002.
- Horn H, Syed N, Lanfermann H, Maurer K and Dierks T (2003). Cerebral networks linked to the event-related potential P300. *Eur Arch Psychiatry Clin Neurosci* 253: 154-159.
- Horowitz SG, Skudlarski P and Gore JC (2002). Correlations and dissociations between BOLD signal and P300 amplitude in an auditory oddball task: a parametric approach to combining fMRI and ERP. *Magn Reson Imaging* 20: 319-325.
- Hudspeth AJ (2000a). Hearing. In: Principles of neural science, 4th ed. (Kandel ER, Schwartz JH and Jessell TM, Eds.), New York: The McGraw-Hill Companies Inc, pp 590-613.
- Hudspeth AJ (2000b). Sensory transduction in the ear In: Principles of neural science, 4th ed. (Kandel ER, Schwartz JH and Jessell TM, Eds.), New York: The McGraw-Hill Companies Inc, pp 614-624.
- Hyde M (1997). The N1 response and its applications. *Audiol Neurootol* 2: 281-307.
- Imig TJ, Irons WA and Samson FR (1990). Single-unit selectivity to azimuthal direction and sound pressure level of noise bursts in cat high-frequency primary auditory cortex. *J Neurophysiol* 63: 1448-1466.
- Ivry RB (1996). The representation of temporal information in perception and motor control. *Curr Opin Neurobiol* 6: 851-857.
- Ivry RB and Spencer RM (2004). The neural representation of time. *Curr Opin Neurobiol* 14: 225-232.
- Jäncke L, Shah NJ, Posse S, Grosse-Ryukun M and Muller-Gartner HW (1998). Intensity coding of auditory stimuli: an fMRI study. *Neuropsychologia* 36: 875-883.
- Jerger J, Weikers NJ, Sharbrough FW 3rd and Jerger S (1969). Bilateral lesions of the temporal lobe. A case study. *Acta Otolaryngol Suppl* 258: 1-51.
- Jerger J, Lovering L and Wertz M (1972). Auditory disorder following bilateral temporal lobe insult: report of a case. *J Speech Hear Disord* 37: 523-535.
- Kaas JH and Hackett TA (1998). Subdivisions of auditory cortex and levels of processing in primates. *Audiol Neurootol* 3: 73-85.
- Kaas JH and Hackett TA (1999). 'What' and 'where' processing in auditory cortex. *Nat Neurosci* 2: 1045-1047.
- Kaas JH, Hackett TA and Tramo MJ (1999). Auditory processing in primate cerebral cortex. *Curr Opin Neurobiol* 9: 164-170.
- Kaas JH and Hackett TA (2000). Subdivisions of auditory cortex and processing streams in primates. *Proc Natl Acad Sci USA* 97: 11793-11799.
- Kanno A, Nakasato N, Fujita S, Seki K, Kawamura T, Ohtomo S, Fujiwara S and Yoshimoto T (1996). Right hemispheric dominance in the auditory evoked magnetic fields for pure-tone stimuli. *Electroencephalogr Clin Neurophysiol Suppl* 47: 129-132.

- Kanno A, Nakasato N, Nagamatsu K, Iwasaki M, Hatanaka K, Murayama N and Yoshimoto T (2001). Comparison of source localization for the P30m, P50m, and N100m peaks of the auditory evoked fields. In: Biomag2000, Proc 12th Int Conf on Biomagnetism (J Nenonen, RJ Ilmoniemi, and T Katila, Eds), Helsinki Univ of Technology, Espoo, Finland, pp 25-28.
- Kanovsky P, Streitova H, Klajblová H, Bares M, Daniel P and Rektor I (2003). The impact of motor activity on intracerebral ERPs: P3 latency variability in modified auditory odd-ball paradigms involving a motor task. *Neurophysiol Clin* 33: 159-168.
- Kanshepolsky J, Kelley JJ and Waggener JD (1973). A cortical auditory disorder. Clinical, audiologic and pathologic aspects. *Neurology* 23: 699-705.
- Karhu J, Herrgård E, Pääkkönen A, Luoma L, Airaksinen E and Partanen J (1997). Dual cerebral processing of elementary auditory input in children. *NeuroReport* 8: 1327-1330.
- Keil A, Bradley MM, Hauk O, Rockstroh B, Elbert T and Lang PJ (2002). Large-scale neural correlates of affective picture processing. *Psychophysiology* 39: 641-649.
- Kiehl KA, Laurens KR, Duty TL, Forster BB and Liddle PF (2001). Neural sources involved in auditory target detection and novelty processing: an event-related fMRI study. *Psychophysiology* 38: 133-142.
- Kirino E, Belger A, Goldman-Rakic P and McCarthy G (2000). Prefrontal activation evoked by infrequent target and novel stimuli in a visual target detection task: an event-related functional magnetic resonance imaging study. *J Neurosci* 20: 6612-6618.
- Kiss I, Dashieff RM and Lordeon P (1989). A parieto-occipital generator for P300: evidence from human intracranial recordings. *Int J Neurosci* 49: 133-139.
- Klingon GH and Bontecou DC (1966). Localization in auditory space. *Neurology* 16: 879-886.
- Knight RT, Hilliard SA, Woods DL and Neville HJ (1980). The effects of frontal and temporal-parietal lesions on the auditory evoked potential in man. *Electroencephalogr Clin Neurophysiol* 50: 112-124.
- Kodera K, Hink RF, Yamada O and Suzuki J (1979). Effects of rise time on simultaneously recorded auditory evoked potentials from the early, middle and late ranges. *Audiology* 18: 395-402.
- Kopp B, Mattler U, Goertz R and Rist F (1996). N2, P3 and the lateralized readiness potential in a nogo task involving selective response priming. *Electroencephalogr Clin Neurophysiol* 99: 19-27.
- Kropotov JD, Alho K, Näätänen R, Ponomarev VA, Kropotova OV, Anichkov AD and Nechaev VB (2000). Human auditory-cortex mechanisms of preattentive sound discrimination. *Neurosci Lett* 280: 87-90.
- Kulikov GA (1994). [Cortical mechanisms in the sensory organization of goal-directed movements][Russian]. *Fiziol Zh Im IM Sechenova* 80: 101-107.
- Kuwada S and Batra R (1999). Coding of sound envelopes by inhibitory rebound in neurons of the superior olivary complex in the unanesthetized rabbit. *J Neurosci Meth* 19: 2273-2287.
- Lammertmann C, Fujiki N, Lütkenhöner B and Hari R (2001). Short-term decrement of the auditory N1m response. In: Biomag2000, Proc 12th Int Conf on Biomagnetism (J Nenonen, RJ Ilmoniemi, and T Katila, Eds), Helsinki Univ of Technology, Espoo, Finland, pp 50-53.
- Lang W, Starr A, Lang V, Lindinger G and Deecke L (1992). Cortical DC potential shifts accompanying auditory and visual short-term memory. *Electroencephalogr Clin Neurophysiol* 82: 285-295.
- Langner G and Schreiner CE (1988). Periodicity coding in the inferior colliculus in the cat. I. Neuronal mechanisms. *J Neurophysiol* 60: 1799-1822.
- Lauter JL, Herscovitch P, Formby C and Raichle ME (1985). Tonotopic organization in human auditory cortex revealed by positron emission tomography. *Hear Res* 20: 199-205.
- Lavikainen J, Huutilainen M, Pekkonen E, Ilmoniemi RJ and Näätänen R (1994). Auditory stimuli activate parietal brain regions: a whole-head MEG study. *NeuroReport* 6: 182-184.
- Lavikainen J, Huutilainen M, Ilmoniemi RJ, Simola JT and Näätänen R (1995). Pitch change of a continuous tone activates two distinct processes in human auditory cortex: a study with whole-head magnetometer. *Electroencephalogr Clin Neurophysiol* 96: 93-96.
- Lavikainen J, Tiitinen H, May P and Näätänen R (1997). Binaural interaction in the human brain can be non-invasively accessed with long-latency event-related potentials. *Neurosci Lett* 222: 37-40.
- Leinonen L, Hyvarinen J and Sovijarvi AR (1980). Functional properties of neurons in the temporo-parietal association cortex of awake monkey. *Exp Brain Res* 39: 203-215.
- Leppert D, Goodin DS and Aminoff MJ (2003). Stimulus recognition and its relationship to the cerebral event-related potential. *Neurology* 61: 1533-1537.

- Lessard N, Lepore F, Poirier P, Villemagne J and Lassonde M (1999). Localization of moving sounds by hemispherectomized subjects. *Behav Brain Res* 104: 37-49.
- Lewis JW, Wightman FL, Brefczynski JA, Phinney RE, Binder JR and DeYoe EA (2004). Human brain regions involved in recognizing environmental sounds. *Cereb Cortex* 14: 1008-1021.
- Lewis JW, Beauchamp MS and DeYoe EA (2000). A comparison of visual and auditory motion processing in human cerebral cortex. *Cereb Cortex* 10:873-888.
- Linden DE, Prvulovic D, Formisano E, Vollinger M, Zanella FE, Goebel R and Dierks T (1999). The functional neuroanatomy of target detection: an fMRI study of visual and auditory oddball tasks. *Cereb Cortex* 9: 815-823.
- Loveless NE, Simpson M and Näätänen R (1987). Frontal negative and parietal positive components of the slow wave dissociated. *Psychophysiology* 24: 340-345.
- Loveless NE (1986). Potentials evoked by temporal deviance. *Biol Psychol* 22: 149-167.
- Lü ZL, Williamson SJ and Kaufman L (1992). Human auditory primary and association cortex have differing lifetimes for activation traces. *Brain Res* 572: 236-241.
- Lütkenhöner B, Krumbholz K and Seither-Preisler A (2003). Studies of tonotopy based on wave N100 of the auditory evoked field are problematic. *NeuroImage* 19: 935-949.
- Maeder PP, Meuli RA, Adriani M, Bellmann A, Fornari E, Thiran JP, Pittet A and Clarke S (2001). Distinct pathways involved in sound recognition and localization: a human fMRI study. *NeuroImage* 14: 802-816.
- Mäkelä JP and Hari R (1990). Long-latency auditory magnetic fields. In: *Advances in Neurology*, vol. 54: Magnetoencephalography (Sato S, Ed.), pp 177-191.
- Maquet P, Lejeune H, Pouthas V, Bonnet M, Casini L, Macar F, Timsit-Berthier M, Vidal F, Ferrara A, Degueldre C, Quaglia L, Delfiore G, Luxen A, Woods R, Mazziotta JC and Comar D (1996). Brain activation induced by estimation of duration: a PET study. *NeuroImage* 3: 119-126.
- Martinkauppi S, Rämä P, Aronen HJ, Korvenoja A and Carlson S (2000). Working memory of auditory localization. *Cereb Cortex* 10: 889-898.
- Martin-Loeches M, and Rubia FJ (1997). Encoding into working memory of spatial location, color, and shape: electrophysiological investigations. *Int J Neurosci* 91: 277-294.
- May P, Tiitinen H, Ilmoniemi RJ, Nyman G, Taylor JG and Näätänen R (1999). Frequency change detection in human auditory cortex. *J Comput Neurosci* 6: 99-120.
- McCallum WC, Barrett K and Pockock PV (1989). Late components of auditory event-related potentials to eight equiprobable stimuli in a target detection task. *Psychophysiology* 26: 683-694.
- McCarthy G, Wood CC, Williamson PD and Spencer DD (1989). Task-dependent field potentials in human hippocampal formation. *J Neurosci* 9: 4253-4268.
- McCarthy G, Luby M, Gore J and Goldman-Rakic P (1997). Infrequent events transiently activate human prefrontal and parietal cortex as measured by functional MRI. *J Neurophysiol* 77: 1630-1634.
- McEvoy LK, Smith ME and Gevins A (1998). Dynamic cortical networks of verbal and spatial working memory: effects of memory load and task practice. *Cereb Cortex* 8: 563-574.
- McLean V, Öhman A and Lader M (1975). Effects of attention, activation and stimulus regularity on short-term 'habituation' of the averaged evoked response. *Biol Psychol* 3: 57-69.
- Mecklinger A and Pfeifer E (1996). Event-related potentials reveal topographical and temporal distinct neuronal activation patterns for spatial and object working memory. *Brain Res Cogn Brain Res* 4: 211-224.
- Mecklinger A, Maess B, Opitz B, Pfeifer E, Cheyne D and Weinberg H (1998). A MEG analysis of the P300 in visual discrimination tasks. *Electroencephalogr Clin Neurophysiol* 108: 45-56.
- Menon V, Ford JM, Lim KO, Glover GH and Pfefferbaum A (1997). Combined event-related fMRI and EEG evidence for temporal-parietal cortex activation during target detection. *NeuroReport* 8: 3029-3037.
- Michel F and Peronnet F (1980). A case of cortical deafness: clinical and electrophysiological data. *Brain Lang* 10: 367-377.
- Michel F, Peronnet F and Schott B (1980). A case of cortical deafness: Clinical and electrophysiological data. *Brain Lang* 10: 367-377.
- Middlebrooks JC (2002). Auditory space processing: here, there or everywhere? *Nat Neurosci* 5: 824-826.
- Middlebrooks JC and Pettigrew JD (1981). Functional classes of neurons in primary auditory cortex of the cat distinguished by sensitivity to sound location. *J Neurosci* 1: 107-120.

- Middlebrooks JC, Clock AE, Xu L and Green DM (1994). A panoramic code for sound location by cortical neurons. *Science* 264: 842-844.
- Middlebrooks JC, Xu L, Eddins AC and Green DM (1998). Codes for sound-source location in nontopographic auditory cortex. *J Neurophysiol* 80: 863-881.
- Middlebrooks JC, Xu L, Furukawa S and Macpherson EA (2002). Cortical neurons that localize sounds. *Neuroscientist* 8: 73-83.
- Milner BA (1962). Laterality effects in audition. In: *Interhemispheric relations and cerebral dominance* (Mountcastle VB, Ed.), Baltimore: John Hopkins Press, pp 177-195.
- Milner BA (1969). Evaluation of the auditory function by computer techniques. *International Audiol* 8: 361-370.
- Mishkin M, Ungerleider LG and Macko KA (1983). Object vision and spatial vision: two cortical pathways. *Trends Neurosci* 6: 414-417.
- Moore KA, Clark CR, Hadfield JL, Brown GC, Taylor DJ, Fitzgibbon SP, Lewis AC, Weber DL and Greenblatt R (2003). Investigating the generators of the scalp recorded visuo-verbal P300 using cortically constrained source localization. *Hum Brain Mapp* 18: 53-77.
- Morosan P, Rademacher J, Schleicher A, Amunts K, Schormann T and Zilles K (2001). Human primary auditory cortex: cytoarchitectonic subdivisions and mapping into a spatial reference system. *NeuroImage* 13: 684-701.
- Morrell LK and Salamy JG (1971). Hemispheric asymmetry of electrocortical response to speech stimuli. *Science* 174: 164-166.
- Näätänen R (1992). *Attention and brain function*. Hillsdale, New Jersey: Lawrence Erlbaum.
- Näätänen R (1982). Processing negativity: An evoked-potential reflection of selective attention. *Psychol Bull* 92: 605-640.
- Näätänen R (1988). Implication of ERP data for psychological theories of attention. *Biol Psychol* 26: 117-163.
- Näätänen R and Alho K (1995). Event-related potentials in human selective attention research. In: *Handbook of Neuropsychology*, vol. 10 (Boller F and Grafman J, Eds.), Elsevier Science, pp 75-104.
- Näätänen R and Gaillard AWK (1983). The N2 deflection of ERP and the orienting reflex. In: *EEG correlates of information processing: Theoretical issues* (Gaillard AWK and Ritter W, Eds.), Amsterdam: North Holland, pp 119-141.
- Näätänen R and Picton TW (1986). N2 and automatic versus controlled processes. *Electroencephalogr Clin Neurophysiol* 38: 169-186.
- Näätänen R and Picton TW (1987). The N1 wave of the human electric and magnetic response to sound: A review and an analysis of the component structure. *Psychophysiology* 24: 375-425.
- Nagahama Y, Okada T, Katsumi Y, Hayashi T, Yamauchi H, Sawamoto N, Toma K, Nakamura K, Hanakawa T, Konishi J, Fukuyama H and Shibasaki H (1999). Transient neural activity in the medial superior frontal gyrus and precuneus time locked with attention shift between object features. *NeuroImage* 10: 193-199.
- Nakasato N, Fujita S, Seki K, Kawamura T, Matani A, Tamura I, Fujiwara S and Yoshimoto T (1995). Functional localization of bilateral auditory cortices using an MRI-linked whole head magnetoencephalography (MEG) system. *Electroencephalogr Clin Neurophysiol* 94: 183-190.
- Nelson DA and Lassman FM (1973). Combined effects of recovery period and stimulus intensity on the human auditory evoked vertex response. *J Speech Hear Res* 16: 297-308.
- O'Leary DS, Andreason NC, Hurtig RR, Hichwa RD, Watkins GL, Ponto LL, Rogers M and Kirchner PT (1996). A positron emission tomography study of binaurally and dichotically presented stimuli: effects of level of language and directed attention. *Brain Lang* 53: 20-39.
- Ohtomo S, Nakasato N, Kanno A, Hatanaka K, Shirane R, Mizoi K and Yoshimoto T (1998). Hemispheric asymmetry of the auditory evoked N100m response in relation to the crossing point between the central sulcus and Sylvian fissure. *Electroencephalogr Clin Neurophysiol* 108: 219-225.
- Oliver DL, Beckius GE, Bishop DC and Kuwada S (1997). Simultaneous anterograde labelling of axonal layers from lateral superior olive and dorsal cochlear nucleus in the inferior colliculus of cat. *J Comp Neurol* 382: 215-229.
- Omoto S, Kuroiwa Y, Li M, Doi H, Shimamura M, Koyano S, Segawa H and Suzuki Y (2001). Modulation of event-related potentials in normal human subjects by visual divided attention to spatial and color factors. *Neurosci Lett* 311: 198-202.
- Onishi S and Davis H (1968). Effects of duration and rise time of tonebursts on evoked V-potentials. *J Acoust Soc Am* 44: 582-591.

- Onitsuka T, Ninomiya H, Sato E, Yamamoto T and Tashiro N (2000). The effect of interstimulus intervals and between-block rests on the auditory evoked potential and magnetic field: is the auditory P50 in humans an overlapping potential? *Clin Neurophysiol* 111: 237-245.
- Onofrij M, Fulgente T, Nobilio D, Malatesta G, Bazzano S, Colamartino P and Gambi D (1992). P3 recordings in patients with bilateral temporal lobe lesions. *Neurology* 42: 1762-1767.
- Owen AM (2000). The role of the lateral frontal cortex in mnemonic processing: the contribution of functional neuroimaging. *Exp Brain Res* 133: 33-43.
- Owen AM, Lee ACH and Williams EJ (2000). Dissociating aspects of verbal working memory within the human frontal lobe: Further evidence for a "process-specific" model of lateral frontal organization. *Psychobiology* 28: 146-155.
- Paavilainen P, Cammann R, Alho K, Reinikainen K, Sams M and Näätänen R (1987). Event-related potentials to pitch change in an auditory stimulus sequence during sleep. *Electroencephalogr Clin Neurophysiol Suppl* 40: 246-255.
- Paavilainen P, Alho K, Reinikainen K, Sams M and Näätänen R (1991). Right-hemispheric dominance of different mismatch negativities. *Electroencephalogr Clin Neurophysiol* 78: 466-479.
- Paller KA, McCarthy G, Roessler E, Allison T and Wood CC (1992). Potentials evoked in human and monkey medial temporal lobe during auditory and visual oddball paradigms. *Electroencephalogr Clin Neurophysiol* 84: 269-279.
- Pandya DN and Seltzer B (1982). Association areas of the cerebral cortex. *Trends Neurosci* 5: 386-390.
- Pantev C, Bertrand O, Eulitz C, Verkindt C, Hampson S, Schuierer G and Elbert T (1995). Specific tonotopic organizations of different areas of the human auditory cortex revealed by simultaneous magnetic and electric recordings. *Electroencephalogr Clin Neurophysiol* 94: 26-40.
- Pantev C, Hoke M, Lehnertz K and Lütkenhöner B (1989). Neuromagnetic evidence of an amplitopic organization of the human auditory cortex. *Electroencephalogr Clin Neurophysiol* 72: 225-231.
- Pantev C, Lütkenhöner B, Hoke M and Lehnertz K (1986). Comparison between simultaneously recorded auditory-evoked magnetic fields and potentials elicited by ipsilateral, contralateral and binaural tone bursts stimulation. *Audiol* 25: 54-61.
- Pantev C, Ross B, Berg P, Elbert T and Rockstroh B (1998). Study of the human auditory cortices using a whole-head magnetometer: left vs right hemisphere and ipsilateral vs. contralateral stimulation. *Audiol Neurootol* 3: 183-90.
- Parasuraman R, Richer F and Beatty J (1982). Detection and recognition: Concurrent processes in perception. *Percept Psychophys* 31: 1-12.
- Pavani F, Macaluso E, Warren JD, Driver J and Griffiths TD (2002). A common cortical substrate activated by horizontal and vertical sound movement in the human brain. *Curr Biol* 12: 1584-1590.
- Pedersen CB, Mirz F, Ovesen T, Ishizu K, Johannsen P, Madsen S and Gjedde A (2000). Cortical centres underlying auditory temporal processing in humans: a PET study. *Audiology* 39: 30-37.
- Pelosi L, Hayward M and Blumhardt LD (1998). Which event-related potentials reflect memory processing in a digit-probe identification task? *Brain Res Cogn Brain Res* 6: 205-218.
- Pelosi L, Holly M, Slade T, Hayward M, Barrett G and Blumhardt LD (1992). Wave form variations in auditory event-related potentials evoked by a memory-scanning task and their relationship with tests of intellectual function. *Electroencephalogr Clin Neurophysiol* 84: 344-352.
- Penhune VB, Zatorre RJ and Feindel WH (1999). The role of auditory cortex in retention of rhythmic patterns as studied in patients with temporal lobe removals including Heschl's gyrus. *Neuropsychologia* 37: 315-331.
- Peretz I (1990). Processing of local and global musical information by unilateral brain-damaged patients. *Brain* 113: 1185-1205.
- Peronnet F, Michel F, Echallier JF and Girod J (1974). Coronal topography of human auditory evoked responses. *Electroencephalogr Clin Neurophysiol* 37: 225-230.
- Perrin F, Maquet P, Peigneux P, Ruby P, Degueldre C, Balteau E, Del Fiore G, Moonen G, Luxen A and Laureys S. (2005). Neural mechanisms involved in the detection of our first name: a combined ERPs and PET study. *Neuropsychologia* 43: 12-19.
- Petrides M (1994). Frontal lobes and working memory: evidence from investigations of the effects of cortical excisions in nonhuman primates. In: *Handbook of neuropsychology*, vol. 9 (Boller F and Grafman J, Eds.) New York: Elsevier, pp 59-82.

- Petrides M and Pandya DN (1988). Association fiber pathways to the frontal cortex from the superior temporal region in the rhesus monkey. *J Comp Neurol* 273: 52-66.
- Pfefferbaum A, Ford JM, Weller BJ and Kopell BS (1985). ERPs to response production and inhibition. *Electroencephalogr Clin Neurophysiol* 60: 423-434.
- Phillips DP, Semple MN, Calford MB and Kitzes LM (1994). Level-dependent representation of stimulus frequency in cat primary auditory cortex. *Exp Brain Res* 102: 210-226.
- Picton TW (1992). The P300 wave of the human event-related potential. *J Clin Neurophysiol* 9: 456-479.
- Picton TW and Hillyard SA (1974). Human auditory evoked potentials. II: Effects of attention. *Electroencephalogr Clin Neurophysiol* 36: 191-199.
- Picton TW, Alain C, Woods DL, John MS, Scherg M, Valdes-Sosa P, Bosch-Bayard J and Trujillo NJ (1999). Intracerebral sources of human auditory-evoked potentials *Audiol Neurootol* 4: 64-79.
- Picton TW, Goodman WS and Bryce DP (1970). Amplitude of evoked responses to tones of high intensity. *Acta Otolaryngol* 70: 77-82.
- Picton TW, Hillyard SA, Krausz HI and Galambos R (1974). Human auditory evoked potentials. I. Evaluation of components. *Electroencephalogr Clin Neurophysiol* 36: 179-190.
- Picton TW, Stapells DR and Campbell KB (1981). Auditory evoked potentials from the human cochlea and brainstem. *J Otolaryngol Suppl* 9: 1-41.
- Picton TW, Woods DL and Proulx GB (1978a). Human auditory sustained potentials. I. The nature of the response. *Electroencephalogr Clin Neurophysiol* 45: 186-197.
- Picton TW, Woods DL and Proulx GB (1978b). Human auditory sustained potentials. II. Stimulus relationships. *Electroencephalogr Clin Neurophysiol* 45: 198-210.
- Pinek B, Duhamel JR, Cave C and Brouchon M (1989). Audio-spatial deficits in humans: differential effects associated with left versus right hemisphere parietal damage. *Cortex* 25: 175-186.
- Polich J and Kok A (1995). Cognitive and biological determinants of P300: an integrative review. *Biol Psychol* 41: 103-146.
- Polich J, Aung M and Dalessio DJ (1988). Long latency auditory evoked potentials: intensity, inter-stimulus interval, and habituation. *Pavlov J Biol Sci* 23: 35-40.
- Ponton C, Eggermont JJ, Khosla D, Kwong B and Don M (2002). Maturation of human central auditory system activity: separating auditory evoked potentials by dipole source modeling. *Clin Neurophysiol* 113: 407-420.
- Ponton CW, Eggermont JJ, Kwong B and Don M (2000). Maturation of human central auditory system activity: evidence from multi-channel evoked potentials. *Clin Neurophysiol* 111: 220-236.
- Pouthas V, Garnero L, Ferrandez AM and Renault B (2000). ERPs and PET analysis of time perception: spatial and temporal brain mapping during visual discrimination tasks. *Hum Brain Mapp* 10: 49-60.
- Pratt H, Michalewski HJ, Barrett G and Starr A (1989a). Brain potentials in a memory-scanning task. I. Modality and task effects on potentials to the probes. *Electroencephalogr Clin Neurophysiol* 72: 407-421.
- Pratt H, Michalewski HJ, Patterson JV and Starr A (1989b). Brain potentials in a memory-scanning task. II. Effects of aging on potentials to the probes. *Electroencephalogr Clin Neurophysiol* 72: 507-517.
- Pratt H, Michalewski HJ, Patterson JV and Starr A (1989c). Brain potentials in a memory-scanning task. III. Potentials to the items being memorized. *Electroencephalogr Clin Neurophysiol* 73: 41-51.
- Prior M, Kinsella G and Giese J (1990). Assessment of musical processing in brain-damaged patients: implications for laterality of music. *J Clin Exp Neuropsychol* 12: 301-312.
- Pugh KR, Shaywitz BA, Shaywitz SE, Fulbright RK, Byrd D, Skudlarski P, Shankweiler DP, Katz L, Constable RT, Fletcher J, Lacadie C, Marchione K and Gore JC (1996). Auditory selective attention: an fMRI investigation *NeuroImage*. 4: 159-173.
- Raij T, McEvoy L, Makela JP and Hari R (1997). Human auditory cortex is activated by omissions of auditory stimuli. *Brain Res* 745: 134-143.
- Rajan R, Aitkin LM, Irvine DR and McKay J (1990). Azimuthal sensitivity of neurons in primary auditory cortex of cats. I. Types of sensitivity and the effects of variations in stimulus parameters. *J Neurophysiol* 64: 872-887.
- Rämä P, Kesseli K, Reinikainen K, Kekoni J, Hämäläinen H and Carlson S (1997). Visuospatial mnemonic load modulates event-related slow potentials. *NeuroReport* 8: 871-876.

- Rämä P, Paavilainen L, Anourova I, Alho K, Reinikainen K, Sipilä S and Carlson S (2000). Modulation of slow brain potentials by working memory load in spatial and nonspatial auditory tasks. *Neuropsychologia* 38: 913-922.
- Rao SM, Mayer AR and Harrington DL (2001). The evolution of brain activation during temporal processing. *Nat Neurosci* 4: 317-323.
- Rauschecker JP and Tian B (2000). Mechanisms and streams for processing of "what" and "where" in auditory cortex. *Proc Natl Acad Sci USA* 97: 11800-11806.
- Rauschecker JP and Tian B (2004). Processing of band-passed noise in the lateral auditory belt cortex of the rhesus monkey. *J Neurophysiol* 91: 2578-2589.
- Rauschecker JP, Tian B and Hauser M (1995). Processing of complex sounds in the macaque nonprimary auditory cortex. *Science* 268: 111-114.
- Rauschecker JP, Tian B, Pons T and Mishkin M (1997). Serial and parallel processing in rhesus monkey auditory cortex. *J Comp Neurol* 382: 89-103.
- Recanzone GH, Guard DC, Phan ML and Su TK (2000). Correlation between the activity of single auditory cortical neurons and sound-localization behavior in the macaque monkey. *J Neurophysiol* 83: 2723-2739.
- Rif J, Hari R, Hämäläinen M and Sams M (1991). Auditory attention affects two different areas in the human supratemporal cortex. *Electroencephalogr Clin Neurophysiol* 79: 464-472.
- Ritter W, Simson R and Vaughan HG Jr (1983). Event-related potential correlates of two stages of information processing in physical and semantic discrimination tasks. *Psychophysiology* 20: 168-179.
- Ritter W, Simson R, Vaughan HG Jr, Friedman D (1979). A brain event related to the making of a sensory discrimination. *Science* 203: 1358-1361.
- Ritter W, Simson R, Vaughan HG Jr and Macht M (1982). Manipulation of event-related potential manifestations of information processing stages. *Science* 218: 909-911.
- Rivier F and Clarke S (1997). Cytochrome oxidase, acetylcholinesterase, and NADPH-diaphorase staining in human supratemporal and insular cortex: evidence for multiple auditory areas. *NeuroImage* 6: 288-304.
- Roberts TP and Poeppel D (1996). Latency of auditory evoked M100 as a function of tone frequency. *NeuroReport* 7: 1138-1140.
- Roberts TPL, Gage N, Ferrari P, Rowley HA and Siegel B (2001). Stimulus dependence of the M100 latency in the age range 11-18 years. In: *Biomag2000, Proc 12th Int Conf on Biomagnetism* (J Nenonen, RJ Ilmoniemi, and T Katila, Eds), Helsinki Univ of Technology, Espoo, Finland, pp 37-39.
- Robin DA, Tranel D and Damasio H (1990). Auditory perception of temporal and spectral events in patients with focal left and right cerebral lesions. *Brain Lang* 39: 539-555.
- Robinson GM and Solomon DJ (1974). Rhythm is processed by the speech hemisphere. *J Exp Psychol* 102: 508-511.
- Rogers RL, Baumann SB, Papanicolaou AC, Bourbon TW, Alagarsamy S and Eisenberg HM (1991). Localization of the P3 sources using magnetoencephalography and magnetic resonance imaging. *Electroencephalogr Clin Neurophysiol* 79: 308-321.
- Rojas DC, Bawn SD, Carlson JP, Arciniegas DB, Teale PD and Reite ML (2002). Alterations in tonotopy and auditory cerebral asymmetry in schizophrenia. *Biol Psychiatr* 52: 32-39.
- Rojas DC, Teale P, Sheeder J, Simon J and Reite M (1997). Sex-specific expression of Heschl's gyrus functional and structural abnormalities in paranoid schizophrenia. *Am J Psychiatry* 154: 1655-1662.
- Romanski LM, Tian B, Fritz J, Mishkin M, Goldman-Rakic PS and Rauschecker J (1999). Dual streams of auditory afferents target multiple domains in the primate prefrontal cortex. *Nature Neurosci* 2: 1131-1136.
- Romanski LM, Tian B, Fritz JB, Mishkin M, Goldman-Rakic PS and Rauschecker J (2000). Reply to "What", "where" and "how" in the auditory cortex". *Nature Neurosci* 3: 966.
- Rosburg T, Kreitschmann-Andermahr I, Emmerich E, Nowak H and Sauer H (1998). Hemispheric differences in frequency dependent dipole orientation of the human auditory evoked field component N100m. *Neurosci Lett* 258: 105-108.
- Rosburg T, Kreitschmann-Andermahr I, Nowak H and Sauer H (2000). Habituation of the auditory evoked field component N100m in male patients with schizophrenia. *J Psychiatr Res* 34: 245-254.
- Rosburg T, Haueisen J and Sauer H (2002). Habituation of the auditory evoked field component N100m and its dependence on stimulus duration. *Clin Neurophysiol* 113: 421-428.

- Roth WT, Ford JM and Kopell BS (1978). Long-latency evoked potentials and reaction time. *Psychophysiology* 15: 17-23.
- Roth WT, Krainz PL, Ford JM, Tinklenberg JR, Rothbart RM and Kopell BS (1976). Parameters of temporal recovery of the human auditory evoked potential. *Electroencephalogr Clin Neurophysiol* 40: 623-632.
- Rothman HH, Davis H and Hay IS (1970). Slow evoked cortical potentials and temporal features of stimulation. *Electroencephalogr Clin Neurophysiol* 29: 225-232.
- Ruchkin DS, Johnson R Jr, Canoune HL, Ritter W and Hammer M (1990). Multiple sources of P3b associated with different types of information. *Psychophysiology* 27: 157-176.
- Ruchkin DS, Johnson R Jr, Grafman J, Canoune H and Ritter W (1992). Distinctions and similarities among working memory processes: an event-related potential study. *Cognit Brain Res* 1: 53-66.
- Ruchkin DS, Johnson R Jr, Mahaffey D and Sutton S (1988). Toward a functional categorization of slow waves. *Psychophysiology* 25: 339-353.
- Ruchkin DS, Sutton S, Kietzman ML and Silver K (1980). Slow wave and P300 in signal detection. *Electroencephalogr Clin Neurophysiol* 50: 35-47.
- Rypma B, Prabhakaran V, Desmond JE, Glover GH and Gabrieli JDE (1999). Load-dependent roles of frontal brain regions in the maintenance of working memory. *NeuroImage* 9: 216-226
- Sanchez-Longo LP and Forster FM (1958). Clinical significance of impairment of sound localization. *Neurology* 8: 119-125.
- Scherg M and von Cramon D (1986). Evoked dipole source potentials of the human auditory cortex. *Electroencephalogr Clin Neurophysiol* 65: 344-360.
- Schreiner CE and Urbas JV (1986). Representation of amplitude modulation in the auditory cortex of the cat. I. The anterior auditory field (AAF). *Hear Res* 21: 227-241.
- Schreiner CE and Urbas JV (1988). Representation of amplitude modulation in the auditory cortex of the cat. II. Comparison between cortical fields. *Hear Res* 32: 49-63.
- Schröger E (1995). Processing of auditory deviants with changes in one versus two stimulus dimensions. *Psychophysiology* 32: 55-65.
- Schröger E and Wolff C (1997). Fast preattentive processing of location: a functional basis for selective listening in humans. *Neurosci Lett* 232: 5-8.
- Shankweiler DP (1961) Performance of brain-damaged patients on two tests of sound localization. *J Comp Physiol Psychol* 54: 375-381.
- Schubotz R and Friederici AD (1997). Electrophysiological correlates of temporal and spatial information processing. *NeuroReport* 8: 1981-1986.
- Simson R, Vaughan Jr, HG and Ritter W (1976). The scalp topography of potentials associated with missing visual or auditory stimuli. *Electroencephalogr Clin Neurophysiol* 40: 33-42.
- Simson R, Vaughan Jr, HG and Ritter W (1977). The scalp topography of potentials in auditory and visual discrimination tasks. *Electroencephalogr Clin Neurophysiol* 42: 528-535.
- Smith DB, Donchin E, Cohen L and Starr A (1970). Auditory averaged evoked potentials in man during selective binaural listening. *Electroencephalogr Clin Neurophysiol* 28: 146-52.
- Smith EE, Jonides J, Koeppel RA, Awh E, Schumacher EH and Minoshima S (1995). Spatial versus object working memory: PET investigations. *J Cogn Neurosci* 7: 337-356.
- Smith ME, Stapleton, JM and Halgren, E (1986). Human medial temporal lobe potentials evoked in memory and language tasks. *Electroencephalogr Clin Neurophysiol* 63: 145-159.
- Smith ME, Halgren E, Sokolik M, Baudena P, Musolino A, Liegeois-Chauvel C and Chauvel P (1990). The intracranial topography of the P3 event-related potential elicited during auditory oddball. *Electroencephalogr Clin Neurophysiol* 76: 235-248.
- Sörös P, Knecht S, Manemann E, Teismann I, Imai T, Lütkenhöner B and Pantev C (2001). Hemispheric asymmetries for auditory short-term habituation of tones? In: *Biomag2000, Proc 12th Int Conf on Biomagnetism* (J Nenonen, RJ Ilmoniemi, and T Katila, Eds), Helsinki Univ of Technology, Espoo, Finland, pp 47-49.
- Sovijarvi AR and Hyvarinen J (1974). Auditory cortical neurons in the cat sensitive to the direction of sound source movement. *Brain Res* Jun 28;73(3): 455-471.
- Spreen O, Benton AL and Fincham RW (1965). Auditory agnosia without aphasia. *Arch Neurol* 13: 84-92.

- Squires NK, Squires KC and Hillyard SA (1975). Two varieties of long-latency positive waves evoked by unpredictable auditory stimuli in man. *Electroencephalogr Clin Neurophysiol* 38: 387-401.
- Starr A, Dong CJ and Michalewski HJ (1996). Brain potentials before and during memory scanning. *Electroencephalogr Clin Neurophysiol* 99: 28-37.
- Stevens AA, Skudlarski P, Gatenby JC and Gore JC (2000). Event-related fMRI of auditory and visual oddball tasks. *Magn Reson Imaging* 18: 495-502.
- Stufflebeam SM, Poeppel D, Rowley HA and Roberts TP (1998). Peri-threshold encoding of stimulus frequency and intensity in the M100 latency. *NeuroReport* 9: 91-94.
- Sutton S, Braren M, Zubin J and John ER (1965). Evoked-potential correlates of stimulus uncertainty. *Science* 150: 1187-1188.
- Sutton S, Tueting P, Zubin J and John ER (1967). Information delivery and the sensory evoked potential. *Science* 155: 1436-1439.
- Swisher L and Hirsh IJ (1972). Brain damage and the ordering of two temporally successive stimuli. *Neuropsychologia* 10: 137-152.
- Takanashi M, Abe K, Yanagihara T, Oshiro Y, Watanabe Y, Tanaka H, Hirabuki N, Nakamura H and Fujita N (2001). Effects of stimulus presentation rate on the activity of primary somatosensory cortex: a functional magnetic resonance imaging study in humans. *Brain Res Bull* 54: 125-129.
- Talavage TM, Ledden PJ, Benson RR, Rosen BR and Melcher JR (2000). Frequency-dependent responses exhibited by multiple regions in human auditory cortex. *Hear Res* 150: 225-244.
- Tarkka IM, Stokic DS, Basile LF and Papanicolaou AC (1995). Electric source localization of the auditory P300 agrees with magnetic source localization. *Electroencephalogr Clin Neurophysiol* 96: 538-545.
- Teale P, Sheeder J, Rojas DC, Walker J and Reite M (1998). Sequential source of the M100 exhibits inter-hemispheric asymmetry. *NeuroReport* 9: 2647-2652.
- Tecchio F, Biccio G, De Campora E, Pasqualetti P, Pizzella V, Indovina I, Cassetta E, Romani GL and Rossini PM (2000). Tonotopic cortical changes following stapes substitution in otosclerotic patients: a magnetoencephalographic study. *Hum Brain Mapp* 10: 28-38.
- Thivard L, Belin P, Zilbovicius M, Poline JB and Samson Y (2000). A cortical region sensitive to auditory spectral motion. *NeuroReport* 11: 2969-2972.
- Thomas CG and Menon RS (1998). Amplitude response and stimulus presentation frequency response of human primary visual cortex using BOLD EPI at 4 T. *Magn Reson Med* 40: 203-209.
- Thompson GC and Masterton RB (1978). Brain stem auditory pathways involved in reflexive head orientation to sound. *J Neurophysiol* 41: 1183-1202.
- Tian B, Reser D, Durham A, Kustov A and Rauschecker JP (2001). Functional specialization in rhesus monkey auditory cortex. *Science* 292: 290-293.
- Tiihonen J, Katila H, Pekkonen E, Jääskeläinen IP, Huotilainen M, Aronen HJ, Ilmoniemi RJ, Räsänen P, Virtanen J, Salli E and Karhu J (1998). Reversal of cerebral asymmetry in schizophrenia measured with magnetoencephalography. *Schizophrenia Res* 30: 209-219.
- Tiitinen H, Alho K, Huotilainen M, Ilmoniemi RJ, Simola J, Näätänen R (1993). Tonotopic auditory cortex and the magnetoencephalographic (MEG) equivalent of the mismatch negativity. *Psychophysiology* 30: 537-540.
- Tiitinen H, Sivonen P, Alku P, Virtanen J and Näätänen R (1999). Electromagnetic recordings reveal latency differences in speech and tone processing in humans. *Brain Res Cogn Brain Res* 8: 355-363.
- Trimble OC (1929). The relative roles of the temporal and intensive factors in sound localization. *Am J Psychol* 41: 564.
- Trimble OC (1935). Intensity-difference and phase-difference as conditions of stimulation in binaural sound localization. *Am J Psychol* 47: 264.
- Tzourio N, Massiou FE, Crivello F, Joliot M, Renault B and Mazoyer B (1997). Functional anatomy of human auditory attention studied with PET. *NeuroImage* 5: 63-77.
- Ungan P, Yagcioglu S and Goksoy C (2001). Differences between the N1 waves of the responses to interaural time and intensity disparities: scalp topography and dipole sources. *Clin Neurophysiol* 112: 485-498.
- Uutela K, Hamalainen M and Somersalo E (1999). Visualization of magnetoencephalographic data using minimum current estimates. *NeuroImage* 10: 173-180.
- Vartanjan IA (1978). [Auditory processing of complex sounds] [Russian], Leningrad: Nauka.

- Vasil'ev AG, Grigor'eva TI and Pavlikova EA (1988). [Characteristics of borderline modulation frequencies in the differentiation of tonal and amplitude-modulated stimuli following the removal of the inferior colliculus in rats] [Russian]. *Zh Vyssh Nerv Deiat Im I P Pavlova* 38: 1119-1125.
- Vaughan HG Jr and Ritter W (1970). The sources of auditory evoked responses recorded from the human scalp. *Electroencephalogr Clin Neurophysiol* 28: 360-367.
- Velasco M and Velasco F (1986). Subcortical correlates of the somatic, auditory and visual vertex activities in man. II. Referential EEG responses. *Electroencephalogr Clin Neurophysiol* 63: 62-67.
- Velasco M, Velasco F and Olvera A (1985). Subcortical correlates of the somatic, auditory and visual vertex activities in man. I. Bipolar EEG responses and electrical stimulation. *Electroencephalogr Clin Neurophysiol* 61: 519-529.
- Verkindt C, Bertrand O, Perrin F, Echallier JF and Pernier J (1995). Tonotopic organization of the human auditory cortex: N100 topography and multiple dipole model analysis. *Electroencephalogr Clin Neurophysiol* 96: 143-156.
- Virtanen J, Ahveninen J, Ilmoniemi RJ, Näätänen R and Pekkonen E (1998). Replicability of MEG and EEG measures of the auditory N1/N1m-response. *Electroencephalogr Clin Neurophysiol* 108: 291-298.
- Vuontela V, Rämä P, Raninen A, Aronen HJ and Carlson S (1999). Selective interference reveals dissociation between memory for location and colour. *NeuroReport* 10: 2235-2240.
- Warren JD and Griffiths TD (2003). Distinct mechanisms for processing spatial sequences and pitch sequences in the human auditory brain. *J Neurosci* 23: 5799-5804.
- Warren JD, Zielinski BA, Green GG, Rauschecker JP and Griffiths TD (2002). Perception of sound-source motion by the human brain. *Neuron* 34: 139-148.
- Watanabe T, Liao TT and Katsuki Y (1968). Neuronal response patterns in the superior olivary complex of the cat to sound stimulation. *Jpn J Physiol* 18: 267-287.
- Weeks RA, Aziz-Sultan A, Bushara KO, Tian B, Wessinger CM, Dang N, Rauschecker JP and Hallett M (1999). A PET study of human auditory processing. *Neurosci Lett* 12: 155-158.
- Wessinger CM, Buonocore MH, Kussmaul CL and Mangun GR (1997). Tonotopy in human auditory cortex examined with functional magnetic resonance imaging. *Human Brain Mapping* 5: 18-25.
- Wessinger CM, VanMeter J, Tian B, Van Lare J, Pekar J and Rauschecker JP (2001). Hierarchical organization of the human auditory cortex revealed by functional magnetic resonance imaging. *J Cogn Neurosci* 13: 1-7.
- Westbury CF, Zatorre RJ and Evans AC (1999). Quantifying variability in the planum temporale: a probability map. *Cereb Cortex* 9: 392-405.
- Wickens CD and Sandry D (1982). Task-hemispheric integrity in dual task performance. *Acta Psychol* 52: 227-247.
- Wilson FAW, O'Scalaidhe SP and Goldman-Rakic PS (1993). Dissociation of object and spatial processing domains in primate prefrontal cortex. *Science* 260: 1955-1957.
- Wolach I and Pratt H (2001). The mode of short-term memory encoding as indicated by event-related potentials in a memory scanning task with distractions. *Clin Neurophysiol* 112: 186-197.
- Woldorff MG (1995). Selective listening at fast stimulus rates: so much to here, so little time. *Electroencephalogr Clin Neurophysiol Suppl* 44: 32-51.
- Wood CC, Goff WR and Day RS (1971). Auditory evoked potentials during speech perception. *Science* 173: 1248-1251.
- Woods DL (1995). The component structure of the N1 wave of the human auditory evoked potential. *Electroencephalogr Clin Neurophysiol Suppl* 44: 102-109.
- Woods DL and Elmasian R (1986). The habituation of event-related potentials to speech sounds and tones. *Electroencephalogr Clin Neurophysiol* 65: 447-459.
- Woods DL, Knight RT and Neville HJ (1984). Bitemporal lesions dissociate auditory evoked potentials and perception. *Electroencephalogr Clin Neurophysiol* 57: 208-220.
- Xu L, Furukawa S and Middlebrooks JC (1998). Sensitivity to sound-source elevation in nontonotopic auditory cortex. *J Neurophysiol* 80: 882-894.
- Yamada K, Kaga K, Uno A and Shindo M (1996). Sound lateralization in patients with lesions including the auditory cortex: comparison of interaural time difference (ITD) discrimination and interaural intensity difference (IID) discrimination. *Hear Res* 101: 173-180.

- Yamada K, Kaga K, Uno A and Shindo M (1997). Comparison of interaural time and intensity difference discrimination in patients with temporal lobe lesions. *Acta Otolaryngol Suppl* 532: 135-137.
- Yamamoto T, Uemura T and Llinas R (1992). Tonotopic organization of human auditory cortex revealed by multi-channel SQUID system. *Acta Otolaryngol* 112(2): 201-204.
- Yang Y, Engelen A, Engelen W, Xu S, Stern E and Silbersweig DA (2000). A silent event-related functional MRI technique for brain activation studies without interference of scanner acoustic noise. *Magn Reson Med* 43: 185-190.
- Yvert B, Bertrand O, Crouzeix A, Seither-Preisler A and Pantev C (2001). EEG/MEG evidence for multiple supratemporal sources of the auditory middle-latency components. In: *Biomag2000, Proc 12th Int Conf on Biomagnetism* (J Nenonen, RJ Ilmoniemi, and T Katila, Eds), Helsinki Univ of Technology, Espoo, Finland, pp 29-32.
- Yvert B, Bertrand O, Pernier J and Ilmoniemi RJ (1998). Human cortical responses evoked by dichotically presented tones of different frequencies. *NeuroReport* 9: 1115-1119.
- Zago L and Tzourio-Mazoyer N (2002). Distinguishing visuospatial working memory and complex mental calculation areas within the parietal lobes. *Neurosci Lett* 331: 45-49.
- Zatorre RJ (1988). Pitch perception of complex tones and human temporal-lobe function. *J Acoust Soc Am* 84: 566-572.
- Zatorre RJ, Bouffard M, Ahad P and Belin P (2002). Where is 'where' in the human auditory cortex? *Nat Neurosci* 5: 905-909.
- Zatorre RJ and Samson S (1991). Role of the right temporal neocortex in retention of pitch in auditory short-term memory. *Brain* 114: 2403-2417.
- Zatorre RJ, Bouffard M and Belin P (2004). Sensitivity to auditory object features in human temporal neocortex. *J Neurosci* 24: 3637-3642.
- Zatorre RJ, Evans AC and Meyer E (1994). Neural mechanisms underlying melodic perception and memory for pitch. *J Neurosci* 14: 1908-1919.
- Zatorre RJ, Mondor TA and Evans AC (1999). Auditory attention to space and frequency activates similar cerebral systems. *NeuroImage* 10: 544-554.
- Zatorre RJ, Ptito A and Villemure JG (1995). Preserved auditory spatial localization following cerebral hemispherectomy. *Brain* 118: 879-889.
- Zhu XH, Kim SG, Andersen P, Ogawa S, Ugurbil K and Chen W (1998). Simultaneous oxygenation and perfusion imaging study of functional activity in primary visual cortex at different visual stimulation frequency: quantitative correlation between BOLD and CBF changes. *Magn Reson Med* 40: 703-711.
- Zurowski B, Gostomzyk J, Gron G, Weller R, Schirmer H, Neumeier B, Spitzer M, Reske SN and Walter H (2002). Dissociating a common working memory network from different neural substrates of phonological and spatial stimulus processing. *NeuroImage* 15: 45-57.