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Pre-Attentive Processing of Sound Duration Changes: Low Resolution Brain Electromagnetic Tomography Study

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1. Introduction

The human central auditory system has a remarkable ability to establish memory traces for invariant features in the acoustic environments in order to correct the interpretation of natural acoustic sound heard. Even when no conscious attention is paid to the surrounding sounds, changes in their regularity can cause the listener to redirect his or her attention toward the sound heard (Tervaniemi *et al.,* 2001). When engaged in a conversation, listeners tune in to the relevant stream of speech and filter out irrelevant speech input that may be present in the same environment. Nonetheless, attention might be involuntarily diverted to meaningful items coming from an ignored stream, like in the well-known own-name effect (Moray, 1959). This brings up the question of to what extent speech is processed in the ignored streams. In the past decade, there have witnessed a resurgence in the electrophysiological literature of attempts to understand how the brain processes the speech signal (Kraus *et al.,* 1993, 1996; Molfese, 1985). One of the most used and well known paradigms in electrosphysiological research is the so-called oddball paradigm, in which typically two stimuli are presented, in random order. One of the stimuli occurs less frequently than the other and the subject is required to discriminate the infrequent stimulus (deviant, target or oddball) from the frequent one (standard). Two main types of ERPs have been described in the literature as a response to the detection of the deviant: P300 and the MMN (Aaltonen *et al.,* 1994; Kraus *et al.,* 1993, 1996). If the subject is required to respond overtly --- for example, by pressing a button – each time he/she detects the deviant, a positive wave peaking approximately 300 ms after deviant onset is elicited. This wave is called P300 and it is largest over electrode sites in normal adults. Such positivity is thought to reflect voluntary focused attention (context updating, response selection). However, if the subject is not required to respond overtly, and one subtracts the event-related potentials (ERPs) obtained in response to the standard, from the ERPs obtained for the deviant, so-called mismatch negativity (MMN) may be observed, usually peaking between 100 and 300 ms after stimulus onset depending on the characteristics of the difference between standard and deviant stimuli. This component is thought to reflect a pre-attentional detection of deviation, a mismatch between the deviant and the memory trace formed by the standard.

Event-related potentials (ERPs) recordings have bought new insight to the neuronal events behind auditory change detection in audition. ERPs components reflect the conscious detection of a physical, semantic, or syntactic deviation from the expected sounds (Tervaniemi *et al.*, 2001). The ERPs recordings thus allow one to probe the neural processes preceding the involvement of the attentional mechanisms. For instances, ERPs have been recorded that reflect memory traces representing sounds composed of several simultaneous or successive tonal elements (Schröger *et al.*, 1996; Alain *et al.*, 1994; Alho *et al.*, 1996). In auditory perception, the occurrence of the deviant (infrequent) stimulus after a sequence of the standard (Frequent) stimuli tends to elicit MMN in event-related potentials (ERPs) and its magnetic equivalent called the magnetic mismatch field (MMF) in magnetoencephalography (MEG). The MMN/MMF component may be considered to reflect the pre-attentive auditory memory processes and represents neuronal correlates of change detection and sound discrimination (Näätänen, 1992). Previous studies showed that for sinusoidal tones, the MMF is sensitive to the direction of a change within the stimulus, being more robustly activated for duration shortening or pitch falling as opposed to lengthening or leveling (Inouchi *et al.*, 2002). These studies also revealed no significant differences between subjects who spoke a pitch-accent language (Japanese) and those who did not (English). It has been reported that MMN/MMF is indeed sensitive to cross-linguistic relevance. Unlike short-to-long vowel duration and falling-to-level pitch changes, long-to-short duration and level-to-falling pitch changes elicited a prominent MMF bilaterally for both groups, peaking at around 100 ms after change onset for duration and 200 ms for pitch. The MMF component is sensitive is sensitive to vowel shortening rather than lengthening and to pitch falling rather than leveling (Inouchi *et al.*, 2002, 2003).

2. Neurophysiological features of mismatch negativity

The search for an objective index of change detection in the human brain can be traced back to 1975, with the proposition that stimulus deviation per se (irrespective of, e.g., stimulus significance, attentional mechanisms) should produce a measurable brain response (Näätänen, 1992). Experimental evidence for this suggestion was obtained in experiments conducted by Näätänen, Gaillard, and Mäntysalo in 1975 (subsequently reported in 1978). In this dichotic listening study, the subject's task was to detect occasional deviant stimuli in the stimulus sequence presented to a designated ear while ignoring the concurrent sequence presented to the opposite ear. The irrelevant stimulus sequence included deviant stimuli that were physically equivalent to the deviant stimuli (targets) of the attended input sequence. The deviant stimuli were either tones of a slightly higher frequency or tones of a slightly greater intensity than the standard tones. A neurophysiological paradigm well suited to examine pre-attentive and automatic central auditory processing is the mismatch negativity (MMN). This is a negative component of the event-related brain potential (ERP), elicited when a detectable change occurs in repetitive homogeneous auditory stimuli (Näätänen, 1992). The most commonly described MMN occurs at 100-300 ms post-stimulus onset although other studies have found later MMNs between 300 and 600 ms (Kraus *et al.*, 1996). The MMN is elicited by any change in frequency, intensity or duration of tone stimuli, as well as by changes in complex stimuli such as phonetic stimuli (Näätänen, 1992). It is assumed to arise as a result of a mechanism that compares each current auditory input with a trace of recent auditory input stored in the auditory memory. The MMN usually reaches its amplitude maximum over the fronto-central scalp (Näätänen, 1992).

The deviant stimuli both in the attended and unattended stimulus sequence elicited negativity in the 100-200 ms latency range, which could not be seen in response to the standard stimuli. This negativity, usually described by the deviant-minus-standard difference wave, was very similar for the attended and ignored input sequences, suggesting that attention was not required. Näätänen *et al.* (1978) proposed that it may well be that a physiological mismatch process caused by a sensory input deviating from the memory trace formed by a frequent background stimulus is such an automatic basic process that it takes place irrespective of the intentions of the experimenter and the subject, perhaps even unmodified by the latter. On the basis of the relatively large MMN amplitudes above the temporal areas, the authors further suggested that the mismatch negativity reflects specific auditory stimulus discrimination processes taking place in the auditory primary and association areas. The latter processes are suggested to be largely automatic, beyond the control of will, instructions, etc. This finding, suggesting the existence of an automatic memory mechanism subsequently paved the way for a series of new experiments where changes in basic stimulus features (frequency, intensity, and duration) and the elicitation of the MMN were addressed in more detail. It was established that the MMN is elicited by both increments and decrements in basic stimulus features. The MMN, however, is not elicited when a stimulus sequence begins or, similarly, when stimuli are presented with very long interstimulus intervals (ISIs). Thus, it was concluded that no stimulus per se is an adequate stimulus for the MMN generator mechanism, as the system responds to the difference between the consecutive stimuli. This response pattern is clearly separable from the behavior of N1 response; the N1 amplitude is largest in response to the first stimulus of a series, strongly attenuating thereafter and showing only partial recovery to a subsequent different stimulus.

Mismatch negativity (MMN), an index of preattentive processing of perceived sounds, is an Event-related Potential (ERP) component elicited by rare deviant stimuli within a sequence of repetitive auditory stimuli. Mismatch negativity component of ERP is theoretically elicited in the auditory cortex when incoming sounds are detected as deviating from a neural representation of acoustic regularities. The mismatch negativity (Näätänen *et al.*, 1978) and its magnetic equivalent (MMNm) are elicited by any discriminable change in some repetitive aspect of auditory stimulation, irrespective of the direction of the subject's attention. It is mainly generated in the auditory cortex (Scherg *et al.*, 1989) occurring between 100 to 250 ms and thus long been regarded as specific to the auditory modality (Näätänen, 1992; Nyman *et al.*, 1990). Additionally, this negative component of the auditory event-related potential (ERPs), usually peaking 100-300 ms from change onset, is based on, and reflects, neural traces by which the auditory cortex models the repetitive aspects of the acoustic past (Näätänen and Winkler 1999). These traces might contain sensory information on sound frequency, duration and inter-stimulus interval (ISI), but also on more complex aspects of auditory stimulation, such as rhythmic patterns or speech sounds (Näätänen and Winkler 1999). The properties of these traces (which usually last several seconds, although even permanent traces can be reflected (Näätänen and Winkler 1999)) can be probed by presenting infrequent deviant events in the sequence of repetitive events ('standard') (Näätänen and Winkler 1999). MMN is elicited even in the absence of attention, for example, in individuals in a coma a few days before the recovery of consciousness (Kane *et al.,* 1993), which indicates that MMN indexes pre-attentive (attention-independent) auditory processing. The automatic change-detection system in the human brain as reflected by the

MMN thus requires the storage of the previous state of the acoustic environment for detecting an incoming deviating sound (Näätänen, 1992; Brattico *et al.*, 2002). Furthermore, MMN implies the existence of an auditory sensory memory that stores a neural representation of a standard against which any incoming auditory input is compared (Ritter et al., 1995). In the auditory modality, MMN is an automatic process which occurs even when the subject's attention is focused away from the evoking stimuli (Näätänen, 1992). Its onset normally begins before the N2b-P3 complex which occurs when attention is directed to the stimuli. The duration of MMN varies with the nature of the stimulus deviance but it invariably overlaps N2b when the latter is present (Tales *et al.*, 1999)

The main neural generators of MMN are bilaterally located in the supratemporal plane (Alho, 1995), which is indicated by dipole modeling (Scherg *et al.*, 1989) and scalp current density map (Giard *et al.*, 1990) of scalp-recorded event-related potentials, as well as by magnetic recordings, intracranial MMN recordings in cats, monkeys and humans, and by positron emission tomography, functional magnetic resonance imaging, and optical imaging data. Furthermore, the exact locus of MMN in auditory cortex depends on the attribute (Giad *et al.*, 1995) (and even on the complexity of stimulus configuration (Alho *et al.*, 1996)) in which the change occurred. Therefore, one can conclude that the auditory processes that generate MMN originate, in the first place, in the auditory cortex. In addition, MMN also receives a contribution from a (mainly right hemispheric) frontal generator that appears to be triggered by this auditory-cortex change-detection process and be associated with the initiation of attention switch to the change (Escera *et al.*, 2000).

The present study compared preattentive brain processes during the discrimination of the different synthesized sounds duration. A single pair of the synthesized long and short sounds selected to represent ideal exemplars. This study chose to record and compared the MMN elicited by these synthesized sounds, hoping to find evidence for specific brain signatures of both synthesized long and short sounds processing in the human auditory cortex. Two questions were examined using this approach: (1) whether the MMN would index differences in the brain's discrimination of this different synthesized sounds duration; and (2) whether the MMN amplitude and/or latency would reflect acoustic differences between the rare deviant and the frequent standard stimuli. Additionally, the low-resolution electromagnetic tomography (LORETA) analysis were used to locate multiple non-dipolar sources particularly involved in the discrimination of these different synthesized sounds duration within the MMN paradigm.

3. Participants, handedness and ethical consideration

EEG recordings were collected from eleven healthy young, Thai-speaking adults (eight female) and their age range: 23-29 years. All participants were right-handedness assessed according to Oldfield (Oldfield, 1971). They had normal hearing, corrected to normal vision and had no history of neurological or psychiatric history. The mean (±sd) age was 25.73 (±3.1) years. The Ethics committees of the involved institutions accepted the study. The concept was explained to the participants, and written informed consent was obtained. All participants gave their written informed consent to participate in the experiments and were paid for their participation. The experiments were performed in accordance with the Helsinki Declaration. Ethical permission for the experiments was issued by the Committee on Human Rights Related to Human experimentation.

The handedness of the participants was assessed with the Edinburgh Handedness Inventory (Oldfield, 1971). The degree of the right handedness of the subjects was assessed based upon ten items; writing; drawing; throwing; scissors; toothbrush; knife (without fork); spoon; broom; striking a match; and open box lid. The participant was instructed to make a "+" on which hand he/she would prefer to use for each action. They were instructed to mark a "++" when the preference was so strong that he/she never used the other hand unassisted. If, in any case, the participant did not have any preference, he/she was instructed to mark a "+" for both hands. The numbers of "+" marked for each hand were totaled. Then, a handedness index was calculated to be the difference of the numbers of "+"'s between the right and left hands divided by the total number of "+"'s for both hands. A handedness index of 1.0 indicated completely right handed, -1.0 corresponded to completely left handed, and 0 suggested ambidextrous. The participant was also asked which foot was preferred for kicking, which eye was preferred when only using one eye, and whether both parents were right handed.

4. General electrophysiological procedures

Two different sounds duration were synthetically generated with short and long sounds. All of the stimuli were digitally edited to have an equal maximum energy level in dB SPL with the remaining intensity level within each of the stimuli scaled accordingly. The stimuli were digitally edited using the Cool Edit Pro v. 2.0 (Syntrillium Software Cooperation) with 500 ms duration (long sound) and 300 ms duration (short sound). All sounds were identical at their frequencies, thus eliminating any effect due to differences in frequency of occurrence of sound. The sounds were presented binaurally via headphones at a comfortable listening level of ~85 dB. The sound pressure levels of stimulus pairs were then measured at the output of headphones using a Brüel and Kjaer 2230 sound level meter. The standard (S)/deviant (D) pairs for each condition were [Condition 1: long-to-short sounds change] Standard/S-(2), Deviant/D-(1), [Condition 2: short-tolong sounds change] S-(1), D-(2). Thus, in both conditions pairs were designed to contrast short and long sounds. The stimuli were presented in a passive oddball paradigm. Deviant stimuli appeared randomly among the standards at 10% probability. Each condition included 125 deviants. The stimuli were binaurally delivered using SuperLab software (Cedrus Corporation, San Pedro, CA, USA) via headphones (Telephonic TDH-39-P). The inter-stimulus interval (ISI) was 1.25 second (offset-onset). EEG signal recording was time-locked to the onset of the sound. Participants were instructed not to pay attention to the stimuli presented via headphones, but rather to concentrate on a self-selected silent movie. Afterwards, they reported the impression of the movie.

Participants are instructed to sit relaxing in comfortable reclining chair in an electrically and acoustically dampened room. They were told that they would participate in the experiment and that the experimenter would be recording their brain electrical activity. They were given written instructions and provided with a grid for their judgements and a pen. They silently read the instructions and at the end the experimenter verifies that everything was clear. Their histories were taken, including age, educational level, handedness, occupation, current medications, medical history (which included past illness, surgical history, head trauma or accident) and history of alcohol consumption or smoking. If there was any significant history of neurological problems, psychiatric problems or head trauma, that participant was excluded. For the Mismatch Negativity (MMN) study, all participants were

instructed to ignore the stimuli by watching a silent, subtitled video of their choice (ignore condition). They were asked to avoid body and eye movements and to keep alert. Before the recording session, the task was explained and a practice block of 50 tones (50 deviants) was presented to the participant to ensure a good level performance. In order to avoid alpha rhythm synchronization during the recording session, participants were instructed to remain with their eyes open while watching a silent, subtitled video of their choice and were instructed to avoid eye movement and blinking. The total experimental session was 1-2 h, including approximately 0.20 h. for electrode placement. During the experimental session, participants took a rest breaks (one 15-min break occurring halfway through the recording session and shorter 5-min breaks as needed). Participants were tested in all experimental conditions on the same day.

5. Electroencephalographic processing

EEG data were collected with a Quick-Cap equipped with 64 channels according to the international 10-20 system using Scan system (Scan 4.3, Neurosoft, Inc. Sterling, USA). Reference electrode was at both ear lobes. The signals were bandpass filtered at 0.05-100 Hz and digitized at 1000 Hz. The impedance of the electrode was below 5 kΩ. Eye movements were monitored with two EOG electrodes. Four electrodes monitored horizontal and vertical eye movements for off-line artifact rejection. Vertical and horizontal electro-oculogram (EOG) was recorded by electrodes situated above and below the left eye, and on the outer canthi of both eyes, respectively. Epochs with EEG or EOG with a large (>100 μV) amplitude were automatically rejected. The artifact-free epochs were filtered at 0.1-15 Hz, baseline corrected and averaged. EEG was segmented into 1000 ms epochs, including the 100 ms pre-stimulus period. The average waveforms obtained from the standard and deviant were digitally filtered by a 0.1 - 15 Hz band-pass filter and finally baseline-corrected. Grand-averaged difference waveforms were calculated by subtracting the standard from the deviant waveforms. For each condition, presence of a prominent MMN was identified by measuring the integrated power amplitudes over the 40-ms time window centered on the MMN peak in the difference waveform. An MMN component was judged prominent if the amplitude difference between standard and deviant within predefined the window was statistically significant. For each participant, the averaged MMN responses contained 125 accepted deviants.

6. Intracerebral distribution of differences in brain electrical activity

In order to visualize and to measure the MMN (deviant-tone ERP-minus-standard-tone ERP difference), after the recording, differences were calculated by subtracting the ERP elicited by the standard tones from that elicited by the corresponding deviant tones of the same stimulus class. The MMN was quantified by first determining the MMN peak latency from the frontal (Fz) grand-average difference waves separately for each deviant. The latency windows for picking up the MMN peaks were predefined on the basis of the across-participants peak latency distribution, determined by visual inspection. The MMN component was defined as the most prominent negative peak within the time windows between 100 and 300 ms. Latency and amplitude figures for waveforms were picked at their point of maximal deflection, as seen at their electrode site of maximal voltage distribution of

frontal (Fz) electrode site. Peak-picking of the prominent peak (MMN) was accomplished by means of moving an 'enhanced point' cursor through the waveforms displayed on the computer screen, while simultaneously paying attention to the resultant changes in the topographic maps. The mean MMN amplitudes at the frontal (Fz) electrode site were calculated as a mean voltage of the 40 ms intervals (so the peak plus minus 20 ms), centered at the corresponding peak latencies of the left and right frontal electrodes in the grand-averaged waveforms, separately for each stimulus type. The amplitudes were determined by using the 100 ms pre-stimulus baseline. When the participants were watching a silent, subtitled video, MMN to spatial acoustic changes was observed as a significant difference between ERPs to the deviant tones and those to the standard tones. It was at its maximum at the frontal (Fz) electrode site consisting of a negative deflection (note that analyses are based on averaged 40-ms blocks of sample points). MMN amplitudes were measured as the mean amplitude over the 100-300 ms period after the stimulus-onset from the deviant-tone ERP-minus-standard-tone ERP differences.

The average MMN latency was defined as a moment of the global field power with an epoch of 40-ms time window related stable scalp-potential topography (Pascual-Marqui, 1994). In the next step, low-resolution electromagnetic tomography (LORETA) was applied to estimate the current source density distribution in the brain, which contributes to the electrical scalp field (Pascual-Marqui *et al.*, 1994). Maps were computed with the Low Resolution Electromagnetic Tomography. Two radically oriented point sources (dipoles) in the brain were selected and computed the 21 channels forward solution electric potential map using a 3-shell unit radius spherical head model. The forward solution maps were then used as input for the LORETA computation in order to test the location precision and the ability of the method to separate the two known dipole locations. Scalp potentials re-referenced to the average reference, excluding the EOG electrodes, were interpolated for mapping using the surface spline method. The CSD maps were computed with the spherical spline interpolated data. The maps were computed at a single time point where the component in question was largest in the grand mean waveforms of each stimulus type and condition separately. LORETA computed the smoothest of all possible source configurations throughout the brain volume by minimizing the total squared Laplacian of source strengths.

Low-resolution Electromagnetic Tomography (LORETA) is the new implementation of LORETA in the Talairach brain. LORETA makes use of the three-shell spherical head model registered to the Talairach human brain atlas (Talairach and Tournoux, 1988), available as a digitized MRI from the Brain Imaging Center, Montreal Neurologic Institute. Registration between spherical and realistic head geometry use EEG electrode coordinates reported by Towle et al. (1993). The solution space is restricted to cortical gray matter and hippocampus, as determined by the corresponding digitized Probability Atlas also available from Brain Imaging Center, Montreal Neurologic Institute. A voxel is labeled as gray matter if it meet the following three conditions: its probability of being gray matter is higher than that of being white matter, its probability of being gray matter is higher than that of being cerebrospinal fluid, and its probability of being gray matter is higher than 33%. Only gray matter voxels at 7-mm spatial resolution are produced under these neuroanatomical constraints. LORETA computations use the exact head model determined from each individual subject's MRI. The final step in any analysis procedure would be to cross-register the individual's anatomical and functional image to the standard Talairach atlas.

The individual momentary potential measures from 21 electrodes at the MMN latency were analyzed with LORETA to determine the MMN source loci (Pascual-Marqui, 1994). These latencies were between 100-140 ms for long- and short-sound duration changes. LORETA calculated the current source density distribution in the brain, which contributed to the electrical scalp field, at each of 2395 voxels in the gray matter and the hippocampus of a reference brain (MNI 305, Brain Imaging Centre, Montreal Neurological Institute) based on the linear weighted sum of the scalp electric potentials (Pascual-Marqui, 1994). LORETA chooses the smoothest of all possible current density configurations throughout the brain volume by minimizing the total squared Laplacian of source strengths. This procedure only implicates that neighboring voxels should have a maximally similar electrical activity, no other assumptions were made. The applied version of LORETA used a three-shell spherical head model registered to the Talairach space and calculated the three-dimensional localization of the electrical sources contributing to the electrical scalp filed for all subjects and conditions, defining the regions of interest on the basis of local maxima of the LORETA distribution. Stereotaxic coordinates of the voxels of the local maxima were determined within areas of significant relative change associated with the tasks. The anatomical localization of these local maxima was assessed with reference to the standard Stereotaxic atlas, and validation of this method of localization was obtained by superimposition of the SPM maps on a standard MRI brain provided by the SPM99. Peaks located within superior temporal gyrus was also identified by using published probability maps following a correction for the differences in the coordinate systems between the Talairach and Tournoux atlas and the Stereotaxic space employed by SPM99.

Regarding to the Brodmann areas(s) and brain regions localization, the Talairach Daemon (TD) will be taken into consideration. The Talairach Daemon (TD) is a high-speed database server for querying and retrieving data about human brain structure over the Internet (http://ric.uthscsa.edu/td_applet/). The TD server data is searched using x-y-z coordinates resolved to 1x1x1 mm volume elements within a standardized stereotaxic space. An array, indexed by x-y-z coordinates, that spans 170 mm (x), 210 mm (y) and 200 mm (z), provides high-speed access to data. Array dimensions are selected to be approximately 25% larger than those of the Co-planar Stereotaxic Atlas of the Human Brain (Talairach and Tournoux, 1988). Coordinates tracked by the TD server are spatially consistent with the Talairach Atlas. Each array location stores a pointer to a relation record that holds data describing what is present at the corresponding coordinate. Presently, the data in relation records are either Structure Probability Maps (SP Maps) or Talairach Atlas Labels, though others can be easily added. The relation records are implemented as linked lists to names and values for brain structures. The TD server is run on a Sun SPARCstation 20 with 200 Mbytes of memory. Intention is to provide 24-hour access to the data using a variety of client applications, as well as continue to add more brain structure information to the database.

7. Statistical evaluation

The statistical significance of MMN (deviant-minus-standard difference) was tested with one-sample *t*-tests by comparing the mean MMN amplitude at the frontal (Fz) electrode site, where the MMN was most prominent. The MMN was measured using the mean frontal (Fz) amplitude in the 100 - 300 ms interval of the deviant-minus-standard difference curves. This interval included the grand mean MMN peak latencies in those conditions where MMN was

elicited. One-sample t- tests were used to verify the presence of the MMN component, by comparing the mean amplitude of the 100 - 300 ms interval against a hypothetical zero, separately in each condition. The MMN latency values was also compared. Repeated measure ANOVA was carried out on the topographic descriptors of the MMN. In order to gather information on cortical sources specifically involved in the MMN generation, LORETA images for deviant sounds were compared with those for standard sounds using paired t-test statistics, after logarithmic transformation of the data. All results were expressed as mean ± S.D and all significant

For the LORETA analyses, the average LORETA images were constructed across participants: the brain electric activity during the ERPs amplitude waveforms for each condition and the voxel-by-voxel t test differences between conditions. The voxel-by-voxel paired t tests were run to assess in which cortical regions the conditions differed. The t maps were threshold at $p < 0.0001$. As pointed out above, reliable differences in the scalp ERP field configuration can unambiguously be interpreted as suggesting that at least partially different neuronal populations are active during the conditions. LORETA assesses in which brain regions the conditions differed. The Structure-Probability Maps Atlas (Lancaster *et al.,* 1997a; 1997b) was also used to determine which brain regions were involved in differences between conditions. Brodmann area(s) (BA) and brain regions closet to the observed locations identified by the Tarairach coordinates were reported. Overall, one sample *P*-values were reported.

8. Pre-attentive processing and lateralization of sound duration changes

The finding indicated that the prominent response to both sounds elicited MMN peaking at 128 to 212 ms from stimulus onset. The grand-averaged ERPs showed that the MMN mean amplitude of both sounds was statistically significant (t-test). The paired sample t-test revealed a significant difference between conditions (t (10) = 73.00; $p < 0.0001$) showing that both sounds equally elicited a MMN. The magnitude of the acoustic difference between the stimulus pairs was reflected by the MMN amplitude, showing larger MMN amplitudes in long sound compared to the short one. The difference in MMN latencies to both sounds might reflect differential processing of the human auditory cortex. The delay in the MMN to the long sound might reflect additional time required to process sound perception. This processing apparently involves activation of a memory trace, or cell assembly, which possibly represents and the processes the sounds.

Estimated source localization of the average MMN responses evoked by both sounds was clearly identified. The current source density values in the time frame 128-212 ms post-stimulus were calculated with LORETA. Stronger activation for long sound was found at 212 ms in the left middle temporal gyrus (MTG) (-59, -32, 1; t-value, 1.81), while the short sound most strongly activated at 128 ms in the left superior temporal gyrus (STG) (-59, -39, 8; t-value, 1.03) (see Figure 1). Analysis of the MMN responses indicated left-hemispheric laterality in both sound durations (F (3,30) = 47.02; $p < 0.0001$). The source analysis indicated strongest MMN response tentatively originating in the left hemisphere and possibly involving the perisylvian area in both sounds, with a more superior distribution for the long sound and a more medial distribution for the short one.
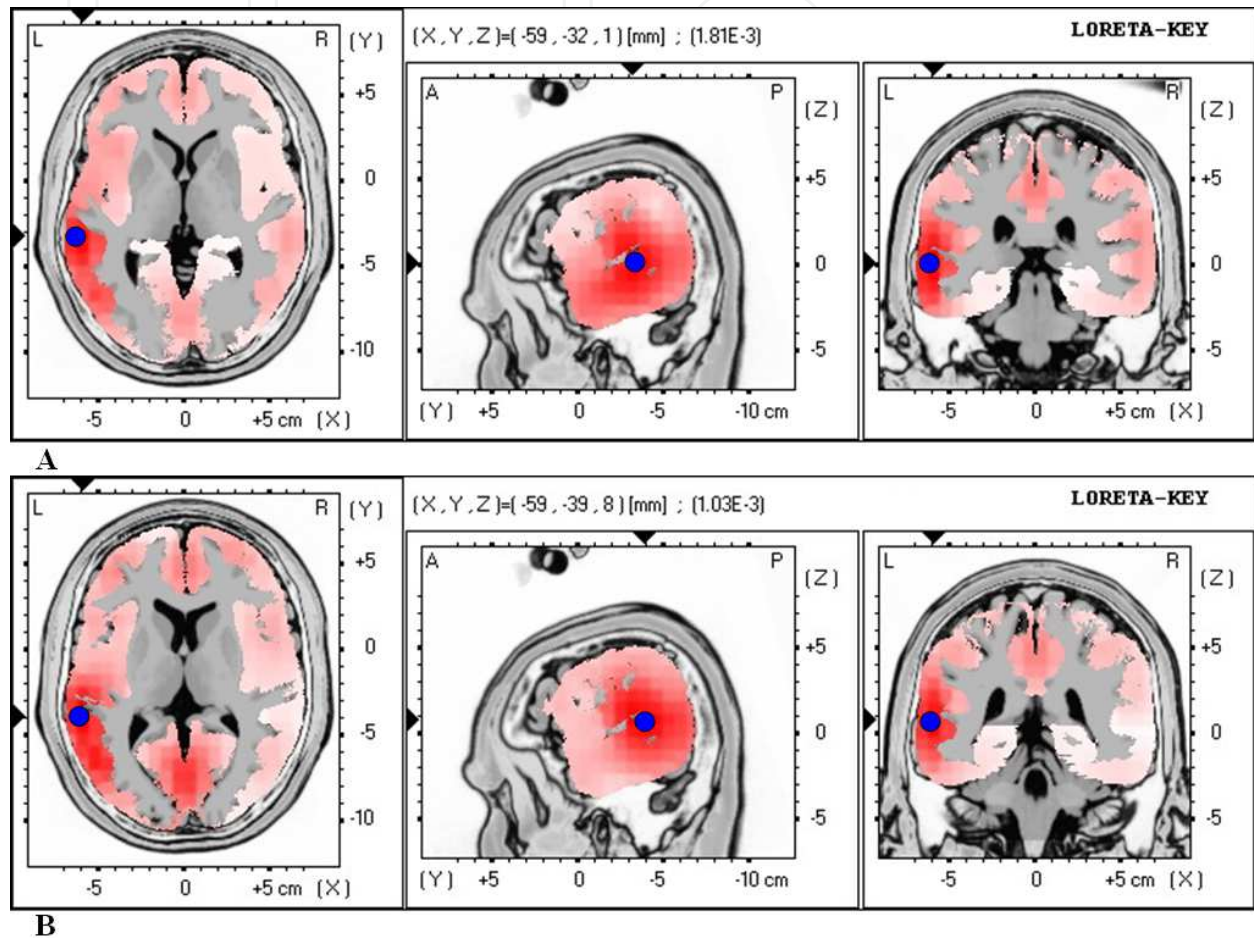
Fig. 1. Graphical representation of the low-resolution electromagnetic tomography (LORETA *t*-statistic comparing the event-related potentials for mismatch negativity (MMN) responses at the time point of the individual peak over Fz for the long sound (A) and short sound (B) activated in the left hemisphere. Red color indicates local maxima of increased electrical activity for both sounds responses in an axial, a saggital and a coronal slice through the reference brain. Blue dots mark the center of significantly increased electric activity.

As it was well established that the MMN amplitude indexes the change detection accuracy (Näätänen, 1999), the MMN to short sound was significantly smaller than those for the long one. The source analysis for the long sound revealed that the source for long sound was located significantly more superior than for short sound in the left hemisphere. In addition, the estimated source strength was not difference between long and short sounds. It is thus the source location rather than its signal strength that might be a primary reason for the reduced responses for short with long sounds. These results may be comparable to those of a previous report by Tiitinen *et al.* (1993) indicating that the MMN sources as well as N100m have a frequency-dependant tonotopy.

Additionally, source analysis suggested MMN sources to be in the vicinity of the left perisylvian area with a more medial distribution for the long deviant and more superior distribution for the short one. It may be that these similar topographies of the neurophysiological brain response do not reflect differential cortical distributions of the underlying neuronal assemblies. The finding of a significantly left-lateralized electric MMN in the present study supports to the previous study indicating a particularly strong asymmetry between the activated neuronal generators in the two hemispheres. There are two possible interpretations for this laterality. First, the functional information tied to the sound no matter of the type of the sounds underlies this laterality. As a second possibility, it may be that it is the functional information related to the stimulus contrasts that is crucial for the strong involvement of left hemispheric processes. Therefore, the MMN response topography and latency in the present study may reveal cortical distribution and activity dynamics of these memory traces. One possible explanation of this hemispheric discrepancy in the MMN effect is that the temporal window of integration (Näätänen and Winkler, 1999; Sussman *et al.,* 1999) differs between two hemispheres. The left hemisphere is suggested to be more sensitive than the right hemisphere to high-frequency temporal patterns of sounds including the stimulus duration. In fact, the perceptual right-ear advantage, regarded as an index of the left hemisphere dominance, can be observed for high-frequency sounds and this advantage is reversed for low-frequency sounds. This may relate to the lack of frequency and duration effect in the right hemisphere, since the long and short distinction mainly rests on the difference of the relatively high frequencies for each of the stimuli. Additionally, the sources for the short stimuli were located more posterior and superior in the left hemisphere than in the right hemisphere. The results replicated previous studies (Alho *et al.,* 1998; Rinne *et al.,* 1999; Tervaniemi *et al.,* 1999). For the source strength of the long and short stimuli, no hemispheric difference was observed. It should be also noted that MMN to short and long sounds showed significant left hemisphere dominance. These results might be in accordance with the findings of Mathiak et al. (1999) rather than studies reporting the left lateralized MMN for speech sounds (Näätänen *et al.*, 1992; Tervaniemi *et al.*, 1999). However, the present study used only one single pair of sounds (i.e., long and short) as an exemplar, which imposes certain limitations on generalization of the current results to all other long and short sounds. Studying this issue using different long and short sounds thus appears to be a fruitful target for further experiments.

9. Conclusion

The prominent MMN component was elicited and more sensitive to the long sound than the short one. The MMN presumably reflect the early stage of processing of different sound

duration in the human brain. So, from the known early auditory-cortex responses to sounds, the MMN reflects an early, pre-attentive, automatic processing of diferent sound duration. The MMN is therefore a potential interest as a technique of evaluating duration of different sounds lateralization, since its measurement is non-invasive, relatively inexpensive (especially in case of the EEG), and applicable to any subjects or patients. The present study has added physiological evidence to earlier psychological and clinico-anatomical evidence that functional characteristics of auditory stimuli differentially influence the brain circuits used at higher cortical stages for processing of different sound duration. Automatic detection of long sound may be a useful index of auditory memory traces of sound perception in the human auditory perception.

10. References

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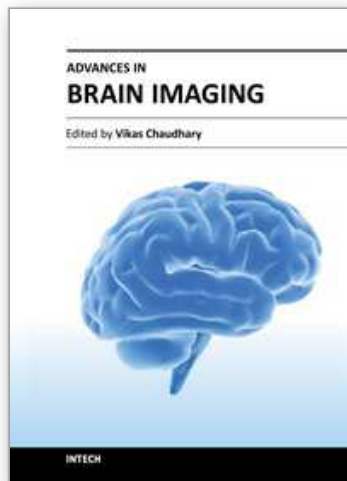
Advances in Brain Imaging

Edited by Dr. Vikas Chaudhary

Remarkable advances in medical diagnostic imaging have been made during the past few decades. The development of new imaging techniques and continuous improvements in the display of digital images have opened new horizons in the study of brain anatomy and pathology. The field of brain imaging has now become a fast-moving, demanding and exciting multidisciplinary activity. I hope that this textbook will be useful to students and clinicians in the field of neuroscience, in understanding the fundamentals of advances in brain imaging.

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