Ultrafast tracking of sound location changes as revealed by human auditory evoked potentials

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ABSTRACT

The rapid discrimination of auditory location information enables grouping and selectively attending to specific sound sources. The typical indicator of auditory change detection is the mismatch negativity (MMN) occurring at a latency of about 100–250 ms. However, recent studies have revealed the existence of earlier markers of frequency deviance detection in the middle-latency response (MLR). Here, we measured the MLR and MMN to changes in sound location. Clicks were presented in either the left or right hemifields during oddball (rare 30°-shifts in location), reversed oddball, and control (sounds occurring equiprobably from five locations) conditions. Clicks at deviant locations elicited an MMN and an enhanced Na component of the MLR peaking at 20 ms compared to clicks at standard or control locations. Whereas MMN was not significantly lateralized, the Na effect showed a contralateral dominance. These findings indicate that, also for sound location changes, early detection processes exist upstream of MMN.

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1. Introduction

Spatial information provides a critical cue to separate auditory objects and plays a crucial role in auditory scene analysis. The extraction of location information enables us to selectively attend to a specific source of auditory input at a given moment in time and to monitor the auditory environment for the occurrence of new sound-emitting objects.

In human electrophysiology, the detection of contextually new or rare auditory features is usually associated with the mismatch negativity (MMN) of the event-related brain potential (ERP). The MMN is a component that is elicited by rare and irregular sounds (termed deviants) occurring in the context of an otherwise repetitive or regular stimulation, irrespectively of the subject's focus of attention (Escera, 2007; Näätänen et al., 1978). Recent theoretical models on novelty and deviance detection and their relation to attention assume that the representation of the incoming stimulus is automatically matched to the predicted sensory information derived from previous stimulus regularities that are held in auditory sensory memory (e.g. Näätänen et al., 2011; Winkler et al., 2009). Importantly, the matching process is supposed to happen on the level of an integrated stimulus representation, i.e. after feature extraction and integration have been completed resulting in

the typical MMN latency between 100 and 250 ms. The neural generators of the MMN have been modeled in the supratemporal cortex of the two hemispheres (Alho, 1995; Huotilainen et al., 1998) and, depending on the paradigm, additionally in frontal areas (Deouell, 2007). Intracranial recordings in animals suggest that MMN-like responses can be observed in different brain structures, including the primary and secondary auditory cortex (Csepe, 1995), the medial geniculate body of the thalamus (Kraus et al., 1994), the inferior colliculus (Csepe, 1995; Malmierca et al., 2009), and also the hippocampus (Ruusuvirta et al., 1995). Based on the findings of single-unit recordings, a property of auditory neurons termed stimulus-specific adaptation (SSA; Antunes et al., 2010; Malmierca et al., 2009; Ulanovsky et al., 2003; von der Behrens et al., 2009) has been proposed as a neural mechanism involved in deviant processing and the generation of MMN (Nelken and Ulanovsky, 2007). An important implication of those studies in animals is the hypothesis that the processing of contextually novel or rare sounds can act at multiple time-scales and different anatomical levels along the auditory pathway starting in the animal model already at about 15 ms after stimulus onset (Pérez-González et al., 2005; von der Behrens et al., 2009). Recent human studies suggest that a similar cascade of deviance detection processes spanning over multiple time scales is at work in the human auditory system. This was shown by Grimm et al. (2011) who reported an enhancement of the Nb component (40 ms after sound onset) of the middle-latency response (MLR) in addition and prior to the elicitation of MMN for rare frequency deviants. A modulation of an MLR component (namely, the Pa component peaking at about 30 ms) through the deviance status of a sound was also reported by Slabu et al. (2010) for deviants

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differing in their spectral content using broadband-filtered noise stimuli.

Other than spectral representations, spatial representations are necessarily computational in the auditory system achieved by analyzing the inputs from the two ears. Dominant mechanisms for sound localization in the horizontal plane are the analyses of interaural time and intensity difference (ITD and IID). Already at the level of the auditory brainstem, the binaural cues are analyzed by ITD and IID-sensitive units (Moore, 1991), still, the auditory cortex has been demonstrated to play an essential role in human sound localization (Zatorre and Penhune, 2001). In the animal model, Reches and Gutfreund (2008) reported SSA for changes in sound location cues (ITD and IID) in mid- and forebrain regions of the barn owl with the difference between standard and deviant responses on average initiating within the first 20 ms after sound onset. In humans, MMN has been widely used to study the detection of location changes (e.g. Doeller et al., 2003; Paavilainen et al., 1989; Röttger et al., 2007; Schröger and Wolff, 1996; Spierer et al., 2007), whereas up to now, only one study investigated effects of automatic location discrimination within earlier time ranges (Sonnadara et al., 2006). The authors report an enhanced Na component (at around 25 ms after sound onset) of the auditory MLR in response to stimuli emitted from a deviant location compared to those emitted from the standard location. However, in the lack of the appropriate control condition (Schröger and Wolff, 1996), one could argue that the responses to standard stimuli observed by Sonnadara et al. (2006) could be reduced per se due to repetition-related refractoriness effects for neurons responding to the standard location (i.e. ITD- and IID-sensitive units, Moore, 1991). Even though early auditory processing in the range of MLR is traditionally thought to show very little refractoriness (Näätänen and Winkler, 1999; Snyder and Large, 2004), several studies have described a reduction of MLR amplitude with sound repetition, for instance in a paired click paradigm (Müller et al., 2001) or in terms of a decreased response amplitude with an increased rate of stimulus repetition (Makeig, 1990). This makes it conceivable that the early deviant-related modulation in comparison to the standard response is the result of repetition-induced refractoriness for the standard and not necessarily that of a memory-based process of deviance detection in that study, though. The distinction of refractoriness-based from genuine regularity-violation-based effects has become crucial when measuring MMN (see Näätänen et al., 2005) and should thus also be applied for earlier deviance-related effects. In the case of early spectral change detection (Grimm et al., 2011; Slabu et al., 2010), deviance-related effects based on a release from refractoriness could be ruled out by a respective control condition (see Schröger and Wolff, 1996) concluding that a memory-based detection mechanism for spectral deviants already affects early levels of auditory processing. Whether this is also the case for the processing of changes in auditory space is still unknown. Therefore, we investigate here the detection of spatial deviants in the time range of the middle-and long-latency response, particularly asking whether early deviance-related responses can be explained by an effect of stimulus probability alone which might reflect release from refractoriness or whether they reflect true deviance processing based on memory traces for the sequence's regularity. Further, we set out to compare the scalp topography of deviance responses dependent on the hemifield of stimulus presentation in order to make inferences on the neural generators that are modulated by stimulus deviance.

2. Materials and methods

2.1. Participants

Twenty healthy volunteers (two men; mean age 19.4 years, range 19–22 years) with no history of neurological disease participated in the study. All subjects gave their written informed consent and were paid 6 €/h. The study was approved by the local ethics committee and performed according to the Declaration of Helsinki. Three subjects had to be excluded from the final analysis due to too few artefact-free trials left after rejection. All included participants had a normal hearing threshold below 20 dB as tested by pure-tone audiometry at the beginning of the experimental session.

2.2. Experimental protocol

Participants were seated in a comfortable chair in an acoustically shielded room in front of a LCD screen. They watched a silent movie with subtitles and were instructed to ignore the auditory stimulation. Five loudspeakers were placed at a distance radius of 1.2 m from the participant at the height of the head at azimuth angles of −60, −30, 0, +30, and +60°. Three infrared LEDs mounted in a plastic headband on the subject's head and an infrared-sensitive camera placed above the subject's head allowed to measure torsional head position. Rotation of the head along the longitudinal axis was captured within the empty interval before each single stimulus presentation with reference to the head position as calibrated at the beginning of the block where subjects were instructed to direct the head to the central loudspeaker. Trials in which head rotations exceeded 1° relative to the preceding trial or 7.5° relative to the reference angle were excluded from further analysis. This was on average for 1.1% of the trials the case.

The experimental protocol consisted of blocks of auditory sequences of five different conditions: (a) an oddball block presented in the left and right hemifield, respectively, (b) a reversed oddball block presented in the left and right hemifield, respectively, (c) a control block presenting tones from all five locations randomly.

Sequences consisted of click sounds (100 μs click length, 60 dB peak-equivalent SPL) separated by a variable stimulus onset asynchrony (SOA) ranging from 195 to 285 ms in ten steps that were equiprobably distributed over trials. In the oddball blocks 80% of the clicks were presented from one loudspeaker (angle of −30° or +30° for the left and right hemifield conditions, respectively), whereas 20% of the clicks were emitted from the loudspeaker placed 30° more lateral (i.e. −60° or +60° for the left and right hemifield conditions, respectively, cf. Fig. 1). In the two reversed oddball conditions the role of the deviant and the standard locations were reversed, so that 80% of the stimuli were emitted from the outer loudspeaker (−/+60°) whereas 20% were emitted from the inner loudspeaker (−/+30°). Stimulus presentation was randomized with the restriction that each deviant was followed by at least two standards. In the control condition, clicks were presented randomly from the five loudspeaker locations, with the restriction that a click could not appear from the same location as in the two preceding trials. In total, 1200 stimuli were presented for each of the six relevant Stimulus Types (left and right deviant, reversed standard, and control stimuli).

2.3. EEG acquisition

The EEG was recorded from 31 electrodes mounted in a Nylon cap (ECI Electro-Cap, Electro-Cap International, Inc., Eaton, OH) at positions Fp1/2, Fpz, F7/8, F3/4, Fz, FC5/6, FC1/2, T7/8, C3/4, Cz, Cp5/6, Cp1/2, P7/8, P3/4, Pz, O1/2, Oz, In1/2 according to the extension of the 10–20 system (Chatrian et al., 1985). Two additional active electrodes were placed at the left and right mastoids. For data acquisition an electrode placed at the tip of the nose served as reference and AFz as ground. The electrooculogram (EOG) was measured bipolarly with two electrodes placed at the outer canthi of the eyes for horizontal EOG (HEOG) and two electrodes placed above and below the right eye for the vertical EOG (VEOG). All channels were continuously digitized at 2 kHz and online filtered between 0.05 and 500 Hz; impedances were kept below 5 kΩ for EEG channels and below 10 kΩ for EOG channels. Offline, data were re-referenced to the combined In1–In2 signal as this gives most robust results for the MLR components (Tooley et al., 2004) because it allows to extract the full amplitude of components including the polarity-inversed portion while introducing little myogenic artefacts.

To analyze long-latency potentials, the EEG was band-pass filtered between 3 and 35 Hz and an independent component analysis (ICA) was applied to correct for eye movement and blink artefacts. Epochs of 500 ms were extracted including a 100-ms baseline prior to stimulus onset. Those epochs containing voltage changes larger than 80 μV were removed from further analysis.

To analyze the stimulus-evoked MLR, the ongoing EEG was band-pass filtered between 15 and 250 Hz. An ICA was applied to remove myogenic artefacts and noise from the continuous filtered data. Data were epoched in 150-ms segments including a 50-ms pre-stimulus baseline. Epochs with voltage changes exceeding 50 μV were removed from further analysis.

Only data from those subjects (N = 17) that had at least 80% artefact-free trials in the evoked responses for each condition analyzed (left and right deviant, reversed standard and control sounds) were included in further analyses. For the final sample, on average 94.6% of the long-latency epochs and 98.8% of the MLR epochs did not exceed the rejection criteria.

For both latency ranges, averages were calculated for the left and right deviants from the oddball blocks (−/+60°), the standards from the reversed blocks (−/+60°), and the corresponding control stimuli (−/+60°).

The Na amplitude was quantified as the mean voltage in a 6-ms time window around the grand-average peak at electrode Fz. In order to define the MMN time