

Cortical and subcortical sides of auditory rhythms and pitches

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It is commonly assumed that different perceptual qualities arising from sensory stimuli depend on their physical nature being transformed by specific peripheral receptors, for example, colour, vibration or heat. A notable unexplained exception is the low and high repetition rates of any sound perceived as rhythm or pitch, respectively. Using auditory discrimination learning in bilaterally auditory cortex ablated animals, we demonstrate that

the perceptual quality of sounds depends on the way the brain processes stimuli rather than on their physical nature. In this context, cortical and subcortical processing steps have different roles in analysing different aspects of sounds with the complete analysis accomplished not before information converges in the auditory cortex. *NeuroReport* 17:853–856 © 2006 Lippincott Williams & Wilkins.

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Introduction

Slow and fast repetitions of sound bursts, physically a continuous class of periodic amplitude modulations of sounds, form discontinuous classes of auditory percepts: when a repetition rate of sounds of any audible spectrum gradually accelerates, the perceived rhythms fuse into hoarse sounds (roughness percept), which then change to tones with rising pitch corresponding to the repetition rate. This pitch is termed 'virtual' because there may be no corresponding frequency component in the sound spectrum (cf. yellow insets in Figs 1 and 2).

Along the auditory pathway, a gradual change of the contribution of two different types of representation of sound periodicity is described: whereas in the auditory nerve all periodicity information is encoded in the temporal pattern of discharges of single fibres, a rate-place code for sound periodicity becomes more and more dominant at levels of the auditory midbrain and higher (cf. [1]), especially for high periodicities [2]. This recoding of periodicity information results in two separate representations for stimulus periodicity in the primary auditory cortex field AI, in which dispersed neurons code for low repetition rates in the range relevant for rhythm perception via temporal phase-locking [2,3] and a map with a special geometry exists of neurons coding for high repetition rates in the range relevant for pitch perception [2,4]. We have argued earlier that these different cortical representations of sound periodicity might underlie the different perceptual qualities evoked by sounds with high and low repetition

rates, respectively [2]. Furthermore, these different cortical codes for stimulus periodicity seem to be reflected in different behavioural performances in a sound periodicity discrimination task [5].

On the basis of these behavioural data and the fact that the periphery of the auditory pathway seems to be superior in the temporal representation of sound periodicities whereas the cortex possesses a highly organized functional map for periodicities, we here follow the hypothesis that the AI contributes differently to the discrimination learning of high and low repetition rates.

To test this hypothesis, we analysed discrimination of repetition rates in Mongolian gerbils with bilaterally ablated auditory cortex. With shuttle-box go/no-go training, we find that lesioned animals can no longer learn to distinguish repetition rates in the virtual pitch range while learning in the rhythm and roughness range remains intact. These results suggest that rhythms are behaviourally accessible already at subcortical levels while accessing virtual pitch information requires an intact auditory cortex.

Methods

All experiments were conducted in accordance with the National Institutes of Health Guidelines for Animals in Research and with the ethical principles defined by the German Law for the protection of experimental animals. The experimental protocols were approved by an ethics committee of the state of Sachsen-Anhalt, Germany.

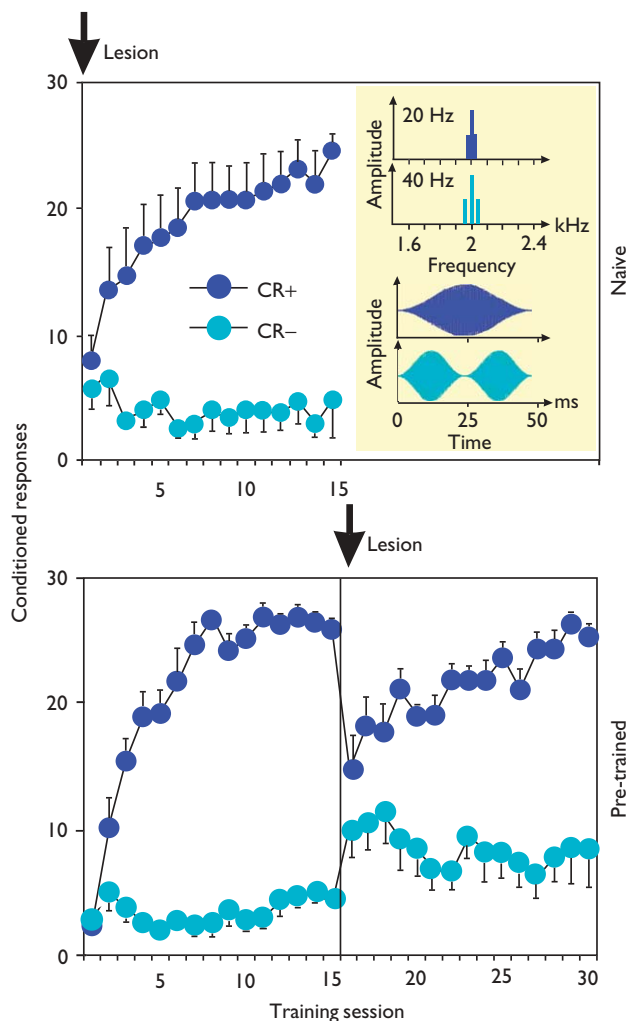


Fig. 1 Discrimination performance of gerbils that received bilateral ablation of auditory cortex before training (top) and of those that were lesioned after 15 days of training (bottom). Animals had to discriminate between two amplitude-modulated tones that differed in modulation frequency (20 vs. 40 Hz); carrier frequency of all sounds: 2 kHz; (cf. yellow inset). Plotted are means and standard errors of conditioned responses (CR) to reinforced (+, dark blue) and non-reinforced (-, light blue) stimuli. Discrimination learning and relearning is still possible after bilateral auditory cortex ablation.

Behavioural training and training groups

A foot-shock-motivated shuttle-box avoidance go/no-go procedure was used for discrimination training of two 100% sinusoidal amplitude modulated tones of different periodicities but identical carrier frequency of 2 kHz. Two groups of gerbils were trained to discriminate periodicities of either 20 vs. 40 Hz or 160 vs. 320 Hz. The lower periodicity always served as the positively reinforced stimulus (conditioned stimulus, CS+), whereas the higher periodicity served as the negatively reinforced stimulus (CS-). In earlier studies, it has been demonstrated that these periodicity pairs are cortically represented by different codes [2], and that also the time course and discrimination performance of discrimination learning differs for these periodicities in the gerbil [5]. Both groups of animals were further divided in one subgroup that was cortically ablated before the first training session (naïve group) and another subgroup that received 15 training sessions before cortex ablation (pre-

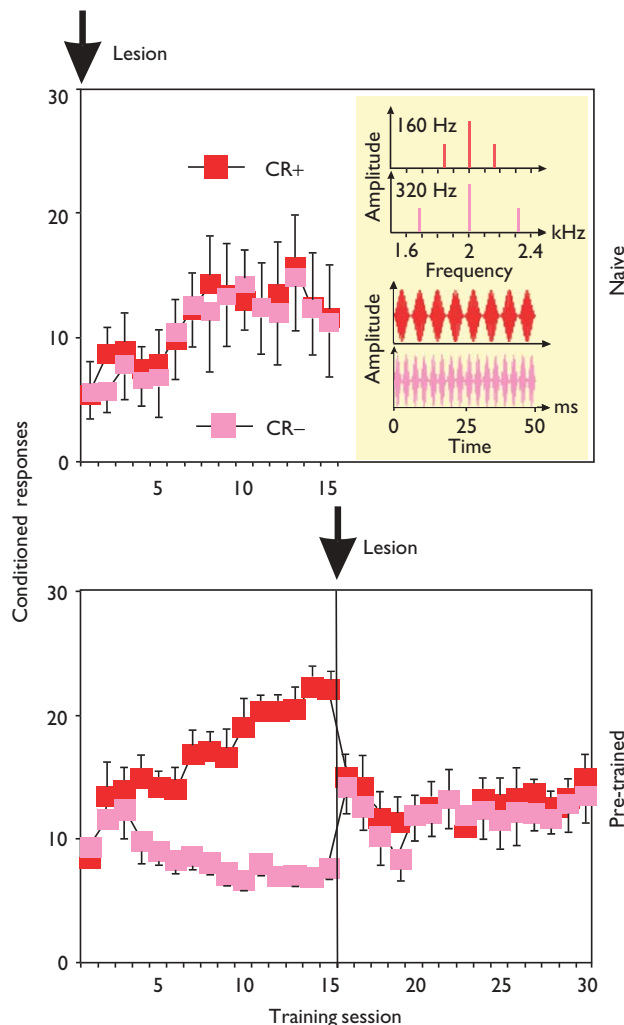


Fig. 2 Discrimination performance of gerbils that received bilateral ablation of auditory cortex before training (top) and of those that were lesioned after 15 days of training (bottom). Animals had to discriminate between two amplitude-modulated tones that differed in modulation frequency (160 vs. 320 Hz); carrier frequency of all sounds: 2 kHz; (cf. yellow inset). Plotted are means and standard errors of conditioned responses (CR) to reinforced (+, dark red) and non-reinforced (-, light red) stimuli. Discrimination learning and relearning is abolished after bilateral auditory cortex ablation.

trained group). Finally, one additional group of animals received bilateral ablations of the organ of Corti to control for possible discrimination on the basis of vibration perception at 20 vs. 40 Hz. Training was carried out as described earlier [5].

Cortical ablation

Similar to earlier studies [6,7], surgery was performed under deep general anaesthesia by an intraperitoneal infusion of ketamine (50 mg/ml; Ratiopharm, Baden-Württemberg, Germany), xylazine (Rompun 2%, BayerVital, Northrhine-Westphalia, Germany) and isotonic sodium chloride solution (mixture 9:1:10) at a rate of 0.06 ml/h, after an initial dose of 0.2 ml. Body temperature was maintained at 37°C using a remote-controlled heating blanket. The skin over the skull and over the temporal bone on both sides was cut and retracted; the musculature covering the temporal bones was

partly removed. The auditory cortex was then exposed by craniotomy and thermocoagulated using a fine tip soldering iron. Finally, the skin over the trepanation area was sealed again using Histoacryl (Braun, Baden-Württemberg, Germany).

Cochlear ablation

Anaesthesia was administered as described for the cortical ablation. Then the skin and muscular tissue over the bulla was cut and retracted on both sides. The organs of Corti were then exposed by drilling small holes (diameter about 1.2 mm) into the bullae and destroyed mechanically with a sterile needle. Finally, the skin over the trepanation area was again sealed using Histoacryl (Braun). These animals were killed with an intrapulmonary injection of T61 (Intervet, Bavaria, Germany) after five training sessions.

Histology

For histological verification of lesion size, Nissl-stained brain sections were obtained from each cortex-ablated animal. After the last training session, animals were killed by an intrapulmonary injection of T61 (Intervet) and then decapitated. The brains were removed, mounted on object slides with 8% gelatin and frozen (-50°C isopentane). Horizontal sections of $40\ \mu\text{m}$ were obtained using a cryostat (-6°C object temperature; -15°C blade temperature) and stained with cresyl violet (cf. [8]). Only animals with a completely ablated auditory cortex in both hemispheres, but without damage of surrounding tissue such as the hippocampus, were included in further analysis of behavioural data ($n=33$).

Results

Data from a total of 33 auditory cortex ablated animals were analysed in this study. Seventeen animals were trained to discriminate periodicities of 20 vs. 40 Hz (eight naïve and nine pre-trained) and 16 to discriminate 160 vs. 320 Hz (seven naïve and nine pre-trained). In addition, three animals were trained to discriminate periodicities of 20 vs. 40 Hz after an initial bilateral ablation of the organs of Corti.

Figure 1 shows average learning curves for animals discriminating 20 vs. 40 Hz periodicities. Conditioned responses (CRs refer to crossing of the hurdle in the shuttle-box paradigm) to the CS+ (dark blue symbols) and to the CS- (light blue symbols) are shown as a function of training session. Obviously, bilaterally cortex lesioned animals are still able to discriminate these slowly amplitude modulated tones, both in the naïve group (top), in which all animals tested learned to significantly discriminate the stimuli, and in the pre-trained group (bottom), in which a re-learning occurred after the lesioning that was successful in eight out of nine animals.

To quantify such learning curves, we used measures of how fast and how well gerbils learned to discriminate between CS+ and CS-: the first session in which the responses to the CR+ were significantly different from those to the CR- on the 1% level (fourfold table χ^2 -test) and which was followed by a session that also fulfilled this criterion served as an index of learning speed. The maximal difference between CR+ and CR- that was reached by each individual gerbil served as the measure of maximal discrimination performance (max DP). Using these measures, no significant differences (Mann-Whitney *U*-test,

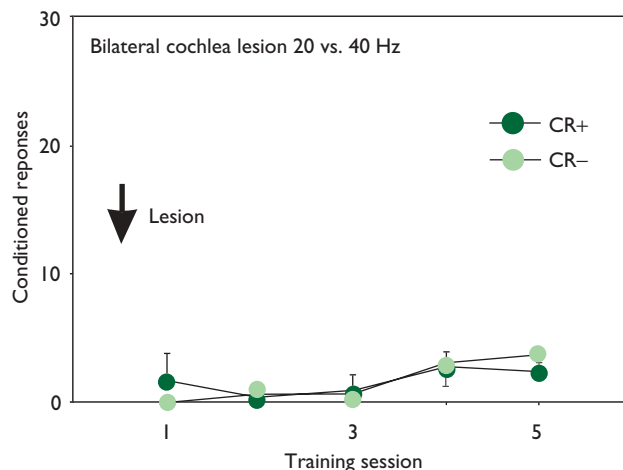


Fig. 3 Discrimination performance of gerbils that received bilateral ablation of organs of Corti before training. Training as in Fig. 1 (top). Plotted are means and standard errors of conditioned responses (CR) to reinforced (+, dark green) and non-reinforced (-, light green) stimuli. Discrimination learning is not possible after bilateral cochlea ablation.

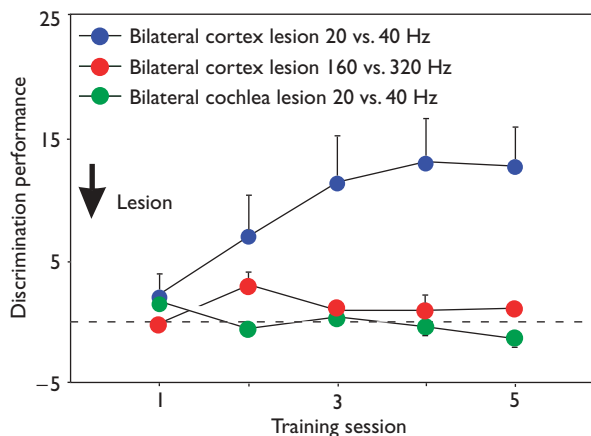


Fig. 4 Comparison of discrimination performance (CR+ vs. CR-) in animals that received lesions before training.

$P > 0.1$) in learning dynamics were found between the naïve and the pre-trained group after lesion (Fig. 1, top, days 1–15 vs. bottom, days 16–30), as well as between lesioned and unlesioned naïve animals (Fig. 1, top vs. bottom, days 1–15, respectively). Although these data indicate that discrimination learning of low repetition rates is possible without an auditory cortex, the cortex still seems to influence discrimination training and performance. This can be inferred from the fact that (1) discrimination performance drops to non-significant levels (χ^2 -test: $P > 0.01$ in seven out of nine animals) in the pre-trained group immediately after lesion, (2) animals that were pre-trained do not reach the same max DP after lesion (mean max DP: before lesion: 26.7, after lesion: 21.0, Mann-Whitney *U*-test, $P < 0.01$) and (3) although not significant, learning speed and performance seem to be slightly better in non-lesioned animals than in lesioned ones [mean learning speed: non-lesioned: 3.1, lesioned (naïve): 3.9, lesioned (pre-trained): 4.25; mean max DP: non-lesioned: 26.7, lesioned (naïve): 23.3].

Lesioned animals were not able to discriminate between stimuli of 160 vs. 320 Hz periodicities (Fig. 2), both in the naïve (top) and in the pre-trained (bottom) groups. Learning, in general, was significantly slower (mean learning speed non-lesioned: 8.2, Mann–Whitney *U*-test, $P < 0.001$) and discrimination performance worse (mean max DP: 19.6, Mann–Whitney *U*-test, $P < 0.001$) than that in the group trained to discriminate low periodicities (Fig. 1) (cf. [5]). Furthermore, after lesioning DP here dropped to zero in the pre-trained group (Fig. 2, bottom) compared with the residual DP seen in Fig. 1 (bottom), suggesting an absence of subcortical components in discrimination learning of high periodicities, that is, the different pitches.

To rule out the potential contribution of vibration information from the somatosensory system to the discrimination performance seen in cortical lesioned animals trained with low periodicities, we carried out identical training with cochlea deafened animals: as can be seen in Fig. 3, such animals could not learn to discriminate the rhythms, although they learned to terminate foot-shock by crossing the hurdle within the first training session.

Discussion

We have demonstrated that naïve and pre-trained animals lose their discrimination ability for periodicities in the virtual pitch range upon bilateral lesioning of the auditory cortex while the discrimination ability for rhythm and roughness declines immediately after lesioning but can be retrained to almost normal levels of performance (Fig. 4).

These findings bear implications for concepts of functional organization of the auditory pathway, namely with respect to cortical and subcortical contributions to discrimination learning and origins of pitch information.

First, our results are compatible with the hypothesis that the known recoding of periodicity information along the auditory pathway, from a synchrony code in the periphery to a central rate–place code, affects the contribution of different levels of auditory processing to discrimination learning of high and low beat rates: an intact auditory cortex is not crucial for discrimination learning of acoustical rhythms and roughness percepts, possibly because this information is represented via a temporal synchronization code throughout the auditory pathway and because this type of coding is particularly well established at subcortical levels.

In agreement with earlier studies [9], discrimination learning of different pitches might require an intact auditory cortex, possibly because an independent representation of these periodicities is not established in the auditory system before the information reaches the auditory cortex. In contrast to the representation of periodicity information via a temporal code (phase locking), a rate or place code for periodicity is not present at the receptor level and auditory nerve. That is, a rate or place code for sound periodicity corresponds to a computational step that has to be generated during the course of neuronal processing along the auditory pathway. A periodicity-map (rate–place code) is first generated at the auditory midbrain (inferior colliculus) level, but in contrast to the cortical periodicity map this representation is not independent of the sound spectrum [1]. In the inferior colliculus, the highest best

modulation frequency (BMF) of a given neuron cannot be higher than one quarter of its characteristic frequency (i.e. $BMF \leq CF/4$). Therefore, we suppose that the remapping of periodicity information between the inferior colliculus and the auditory cortex, which results in a periodicity map independent of the representation of the sound spectrum in a tonotopic map in the auditory cortex [4], is crucial for an unambiguous determination of virtual pitch information. These interpretations are in harmony with the findings that discrimination of frequencies (i.e. the spectral pitches of pure tones) is still possible without auditory cortex [6,10]. For a pure tone pitch, there are no ambiguities between spectral and temporal representations and tonotopic maps are present throughout the auditory pathway up to AI.

Conclusions

We demonstrated that discrimination of low repetition rates of sounds that are perceived as rhythm or roughness is possible without an auditory cortex while the discrimination of high repetition rates in the virtual pitch range requires an intact auditory cortex. Hence, a physical continuum of repetition rates of sounds leads to very different perceptual qualities depending on the processes (spectral vs. temporal) and locations (subcortical vs. cortical) in the auditory pathway responsible for the generation of the percepts.

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