Supporting Information

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SI Materials and Methods

Animals. The study began with 76 female mice (*Mus musculus*, outbred strain NMRI) housed in standard laboratory cages with free access to food (rodent pellets) and water. At the beginning of the experiments all animals were 8 weeks old. The reported data are from 73 animals that turned out to be successful learners, as defined in *Data Analysis* below.

Apparatus and Training Procedure. A two-compartment shuttle-box (16 × 20 × 23 cm) for small rodents (Coulbourn Instruments) with a hurdle 2.5 cm high separating the compartments was used for the conditioning experiments. An electrical foot shock of 100–300 μA applied through the floor grid served as an unconditioned stimulus (UCS). The current level of the shock was adjusted individually to produce a mild escape response in the animals. The animals learned to avoid the foot shock by crossing the hurdle within 4 s after the onset of one of the sounds to be discriminated. The sound to be associated with a go response (CR^+) was named the positively reinforced conditioned stimulus (CS^+). A different sound required the animals to avoid the foot shock by not crossing the hurdle. The sound to be associated with a no-go response (CR^-) was named the negatively reinforced conditioned stimulus (CS^-). Training was carried out over 15 or 30 days with one daily session. A session consisted of 60 trials with 30 randomized presentations of each of the conditioned stimuli (CS^+, CS^-). Interstimulus intervals lasted 15 s.

The sound stimuli were digitally synthesized on a PC (44.1-kHz sampling rate, 16-bit dynamic range; Intel Pentium 4, ASUS) with a duration of 400 ms (including 5-ms rise and fall times) and a repetition rate of 2 Hz. After amplification, stimuli were delivered by a loudspeaker (microphone, microphone power supply, and amplifier; Brüel & Kjær models 4135, 2633, and 2636, respectively) placed at the top of each shuttle-box compartment. The sound pressure level of all sounds presented was calibrated to 70 ± 5 dB at the floor level of the shuttle-box.

The animals could show four types of responses to the CS^+ and CS^- presentations. (*i*) Hurdle crossing within 4 s after onset of the CS^+ was considered a hit (CR^+). The CS^+ presentation was stopped as soon as the hurdle was crossed, and no UCS was delivered. (*ii*) A miss was noted when the animal did not cross the hurdle within 4 s after the onset of the CS^+. In that case, the CS^+ was continued together with an UCS presentation for maximally another 4 s to stimulate the animal to cross the hurdle. (*iii*) A false-alarm (CR^-) was noted when the animal crossed the hurdle during the 4-s CS^- presentation. In that case the animal received an UCS in the compartment to which it had crossed (0.5-s error-shock of 0.5 s) (4). A correct rejection was noted when the animal remained in the compartment during the 4-s presentation of the CS^-. Because there always were 60 trials in every training session, with 30 presentations of CS^+ and CS^-, respectively, there was no need to present the number of correct rejections and misses separately, because these results could be determined from the number of false alarms (number of correct rejections = 30 – CR^-) and from the number of hits (number of misses = 30 – CR^+). All data about stimuli and responses were stored for off-line analysis.

The first experimental group of mice (group A1) was trained to discriminate between pure tones (PT) (CS^+: 12 kHz; CS^-: 7 kHz). Three groups of mice (A2, A3, and A4) were trained to discriminate between modulation frequencies (CS^+: 20 Hz, CS^-: 40 Hz) of 100% sinusoidally amplitude-modulated tones (AM) which could have one of three different carrier frequencies (7 kHz, 9 kHz, or 12 kHz). Three groups of mice (B1, B2, and B3) were trained first for 15 days in the PT paradigm and then were trained for another 15 days in one of the AM paradigms. Another three groups of mice (C1, C2, and C3) were trained first for 15 days in one of the AM paradigms and then were trained for another 15 days in the PT paradigm. Training schedules and animal numbers of the experimental groups are listed in Table S1.

Choice of Stimuli. The study was designed to test the possible transfer of knowledge between tasks in which the sound stimuli to be discriminated were from physically and perceptually different classes with the additional requirement of one discrimination being easy and the other being hard. The discrimination of the pure tones of 7 and 12 kHz should be a rather easy perceptual task in the frequency domain for mice, comparable to the discrimination of 1.7 and 3 kHz in humans; the pairs of frequencies are equivalent for the respective species if one considers the cochlear basilar membranes of mammals as scale models (1, 2). The discrimination of the AM rates of 20 and 40 Hz should be a more difficult task. Humans perceive an AM rate of 20 Hz either as a fast rhythm or as roughness of a carrier frequency, depending on the carrier frequency. An AM rate of 40 Hz produces a roughness percept (3). The perceptions of rhythm and roughness result from a time domain analysis in the auditory system (4). Thus, the mice had to do two different tasks with physically and perceptually different pairs of stimuli.

Data Analysis. Only successful learners were included in the data analysis. Successful learners were defined as animals that reached a criterion of significant ($P < 0.05$, χ^2 test) differences between the rates of CR^+ and CR^- for at least three sessions in a row during the first 15 training sessions. Of the 76 animals with which we started the study, three (one animal each from groups A1, A2, and A4) did not reach this criterion and were excluded from the data analysis. For every training session and experimental group, group means with SD were calculated from individual CR^+ and CR^- response rates (hits and false alarms) as well as the average $d' = z(CR^+ \text{ rate}) - z(CR^- \text{ rate})$ according to signal detection theory (5). The group means of CR^+ and CR^- rates from a given training session were tested for statistically significant differences by using the Mann–Whitney *U* test. In addition, the significance of discrimination performance in every training session was tested for each individual animal by using the rates of the four responses to the CS^+ and CS^- stimuli in a χ^2 test. In all these tests, significance levels of $P < 0.05$, $P < 0.01$, $P < 0.001$ were applied and are indicated in the figures. The development of d' over the training sessions was approximated by linear regressions, the statistical significance of which was expressed via the correlation coefficient *r*. In principle, learning curves can be approximated by a logistic function with five free parameters, but the interpretation of the data is much more difficult with such an approximation than with a linear approximation. Because the learning curves of AM discrimination, as expressed by the d' values, followed linear regressions better than logistic curves (Figs. 2, 3*D*, and 4*D*), we used linear regressions to compare learning speeds of PT and AM discrimination learning. The slopes of the regression lines were tested for significant differences following methods in ref. 6.

Learning performance was quantified further in cluster analyses with discrimination performance and learning speed as the variables (7). Discrimination performance was characterized as the average of the maximal difference between the rates of CR^+ and CR^- responses of each mouse of a group. Learning speed was characterized for each individual mouse by the first session of significant discrimination ($P < 0.05$) in the χ^2 test followed by at least one subsequent session in which this criterion for discrimination also was fulfilled. The data of the cluster analyses were tested for significant differences between the groups by using the Mann–Whitney *U* test. Two animals in group C1 did not reach the criterion for significant discrimination in the χ^2 test and therefore could not be included in the cluster analysis. For this reason and because of the general difference in the data taken to characterize discrimination performances (average CR^+ and CR^+ rates vs. averages of individual performances), statements about learning and learning progress based on the different methods of data evaluation may differ in details.

Also, we tested for possible differences in PT discrimination performance between group A1 and groups B1, B2, and B3 by comparing the slopes and *y*-intercepts of the linear regression lines fitted to the late shallow increases of the d' functions of these groups (2). There were no significant differences in all of the tests (slopes: A1 vs. B1: $P = 0.36$; A1 vs. B2: $P = 0.20$; A1 vs. B3: $P = 0.78$; *y*-intercepts: A1 vs. B1: $P = 0.48$; A1 vs. B2: $P = 0.09$; A1 vs. B3: $P = 0.34$). In addition, we compared the differences between CR^+ and CR^- between each of the groups A1, B1, B2, and B3 separately for all 15 test days (Mann–Whitney *U* test). Again no statistical differences occurred at any day.

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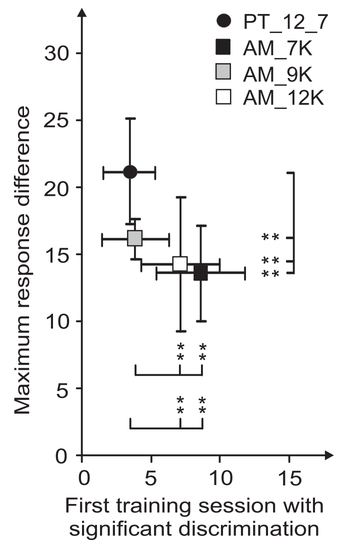

Fig. S1. Differences in learning performance among groups A1–A4, as estimated by measures of learning speed and maximal discrimination performance. Note that, in contrast to the results shown in Fig. 1, this measure of learning speed was calculated from the individual data of each subject and not from group data (*SI Materials and Methods*). Again, the PT group (group A1, black circle) was significantly faster in reaching significant response differences and showed a larger maximal response difference than the AM groups A2 (black square) and A4 (open square). Interestingly, the AM group A3 (gray square) was as fast as the PT group A1 in reaching significant discrimination performance and thus was faster than the other two AM groups A2 and A4. **, $P < 0.01$.

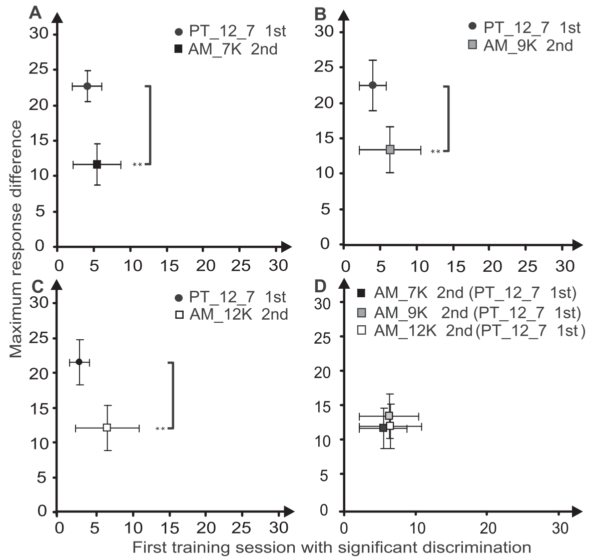

Fig. S2. (*A*–*C*) Comparison between discrimination performance in the first (PT) and the second (AM) training tasks of the groups B1 (AM 7 kHz) (*A*), B2 (AM 9 kHz) (*B*), and B3 (AM 12 kHz) (*C*). The animals always were significantly better in their performance level but were not faster in learning in the PT task compared with the AM task. (*D*) Comparison among groups of discrimination performance in the second (AM) task, as estimated by measures of learning speed and maximal discrimination performance. Learning speed and maximal discrimination performance do not differ among the AM tasks. **, $P < 0.01$.

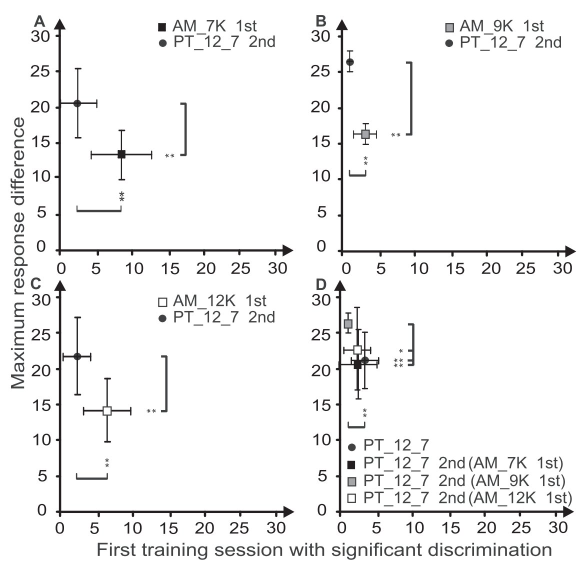

Fig. S3. (*A*–*C*) Comparison of discrimination performance between the first (AM) and the second (PT) training task of the groups C1–C3. The animals are always significantly better in their performance level and faster in learning in the PT task than in the AM task. (*D*) Comparison of the discrimination performance in the second (PT) task among the groups, as estimated by measures of learning speed and maximal discrimination performance. The animals are better in performance and faster in learning the PT discrimination after the AM 9-kHz discrimination task than after the AM 7-kHz or the AM 12-kHz discrimination task. *, $P < 0.05$; **, $P < 0.01$.

Table S1. Training tasks and animal numbers (only for animals included in data analyses)

Group	Paradigm 1	Paradigm 2	Number of animals
A1	PT (7 vs. 12 kHz)	none	32[†]
A2	AM (fc = 7 kHz) (fm = 20 vs. 40 Hz)	none	10[‡]
A3	AM (fc = 9 kHz) (fm = 20 vs. 40 Hz)	none	10[¶]
A4	AM (fc = 12 kHz) (fm = 20 vs. 40 Hz)	none	21[§]
B1	PT (7 vs. 12 kHz)	AM (fc = 7 kHz) (fm = 20 vs. 40 Hz)	8
B2	PT (7 vs. 12 kHz)	AM (fc = 9 kHz) (fm = 20 vs. 40 Hz)	8
B3	PT (7 vs. 12 kHz)	AM (fc = 12 kHz) (fm = 20 vs. 40 Hz)	11
C1	AM (fc = 7 kHz) (fm = 20 vs. 40 Hz)	PT (7 vs. 12 kHz)	10
C2	AM (fc = 9 kHz) (fm = 20 vs. 40 Hz)	PT (7 vs. 12 kHz)	8
C3	AM (fc = 12 kHz) (fm = 20 vs. 40 Hz)	PT (7 vs. 12 kHz)	13

Total number of animals: 73.

[†]Data from all animals of the B groups were also included in the dataset of A1.

[‡]Data from all animals of the C1 group were also included in the dataset of A2.

[¶]Data from all animals of the C2 group were also included in the dataset of A3.

[§]Data from all animals of the C3 group were also included in the dataset of A4.