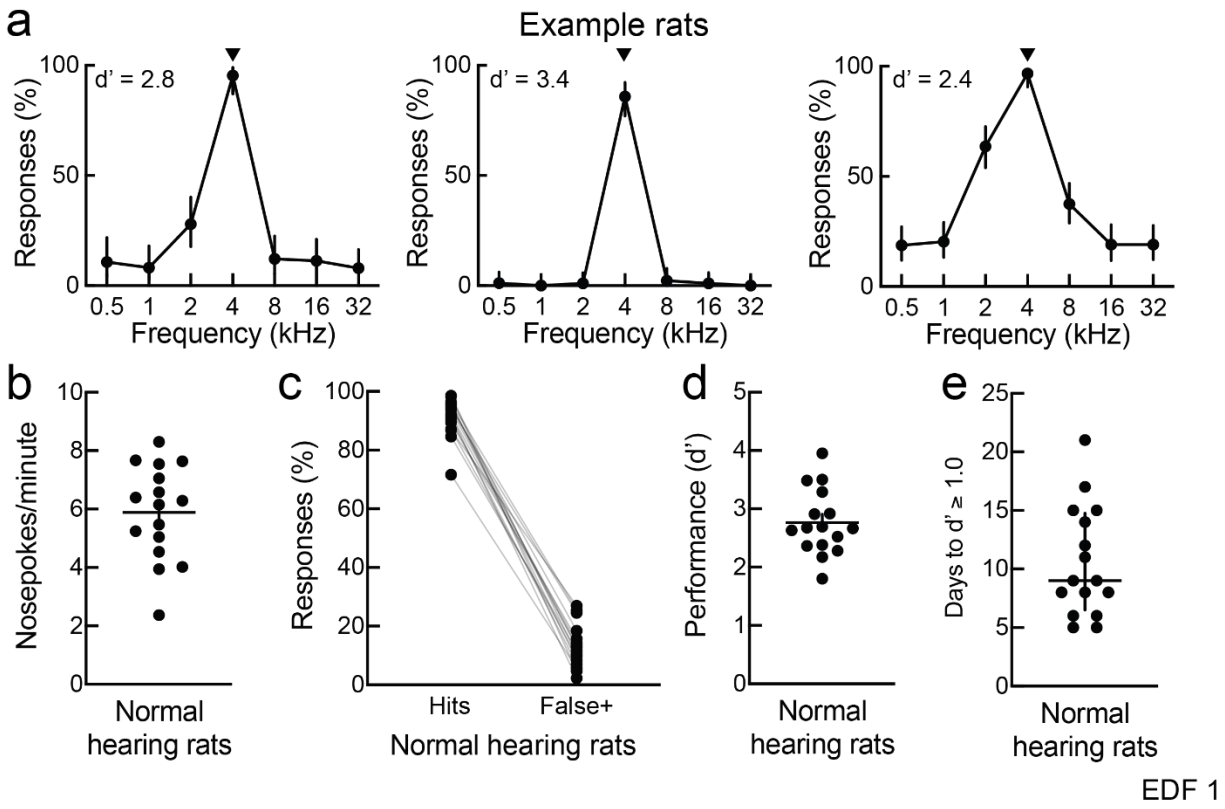
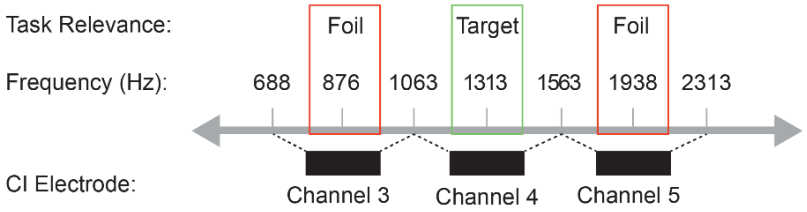
Extended Data Figures and Legends



Extended Data Figure 1. Auditory conditioning on go/no-go task in normal-hearing rats. a, Normal-hearing behavioral response curves from three example rats that reached training criteria. Arrowhead, target tone was 4 kHz for all animals. Error bars, 95% confidence intervals. **b,** Average initiation rates for final five days of normal-hearing behavioral performance (N = 16). Error bars, mean ± s.e.m. **c,** Average hits and false positive rates for final five days. **d,** Average behavioral performance (d') for final five days. Error bars, mean ± s.e.m. **e,** Days to d' ≥ 1.0. Error bars, median ± interquartile range.

a



b

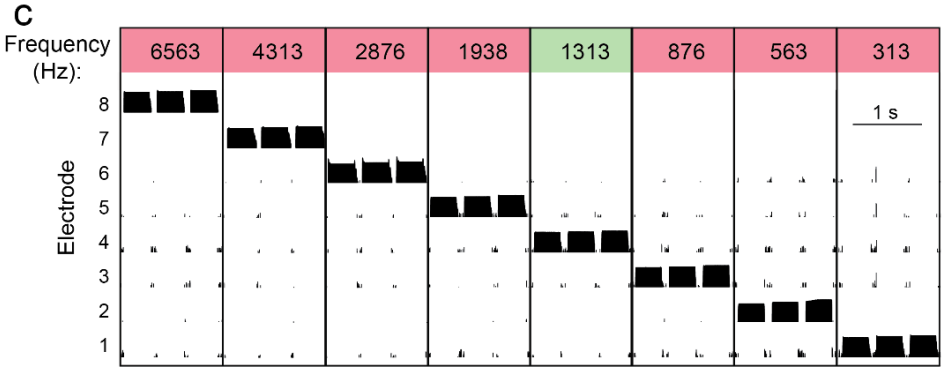
Frequency allocation table 8 channel CI			
Electrode	Lower Frequency	Center Frequency	Upper Frequency
1	188	313	438
2	438	563	688
3	688	875.5	1063
4	1063	1313	1563
5	1563	1938	2313
6	2313	2875.5	3438
7	3438	4313	5188
8	5188	6563	7938

Frequency allocation table 7 channel CI			
Electrode	Lower Frequency	Center Frequency	Upper Frequency
1	188	375.5	563
2	563	813	1063
3	1063	1313	1563
4	1563	1938	2313
5	2313	2900.5	3488
6	3488	4338	5188
7	5188	6563	7938
8	x	x	x

Frequency allocation table 6 channel CI			
Electrode	Lower Frequency	Center Frequency	Upper Frequency
1	188	375.5	563
2	563	813	1063
3	1063	1438	1813
4	1813	2375.5	2938
5	2938	3875.5	4813
6	4813	6375.5	7938
7	x	x	x
8	x	x	x

Frequency allocation table 5 channel CI			
Electrode	Lower Frequency	Center Frequency	Upper Frequency
1	188	963	1738
2	1738	2513	3288
3	3288	4063	4838
4	4838	5613	6388
5	6388	7163	7938
6	x	x	x
7	x	x	x
8	x	x	x

c



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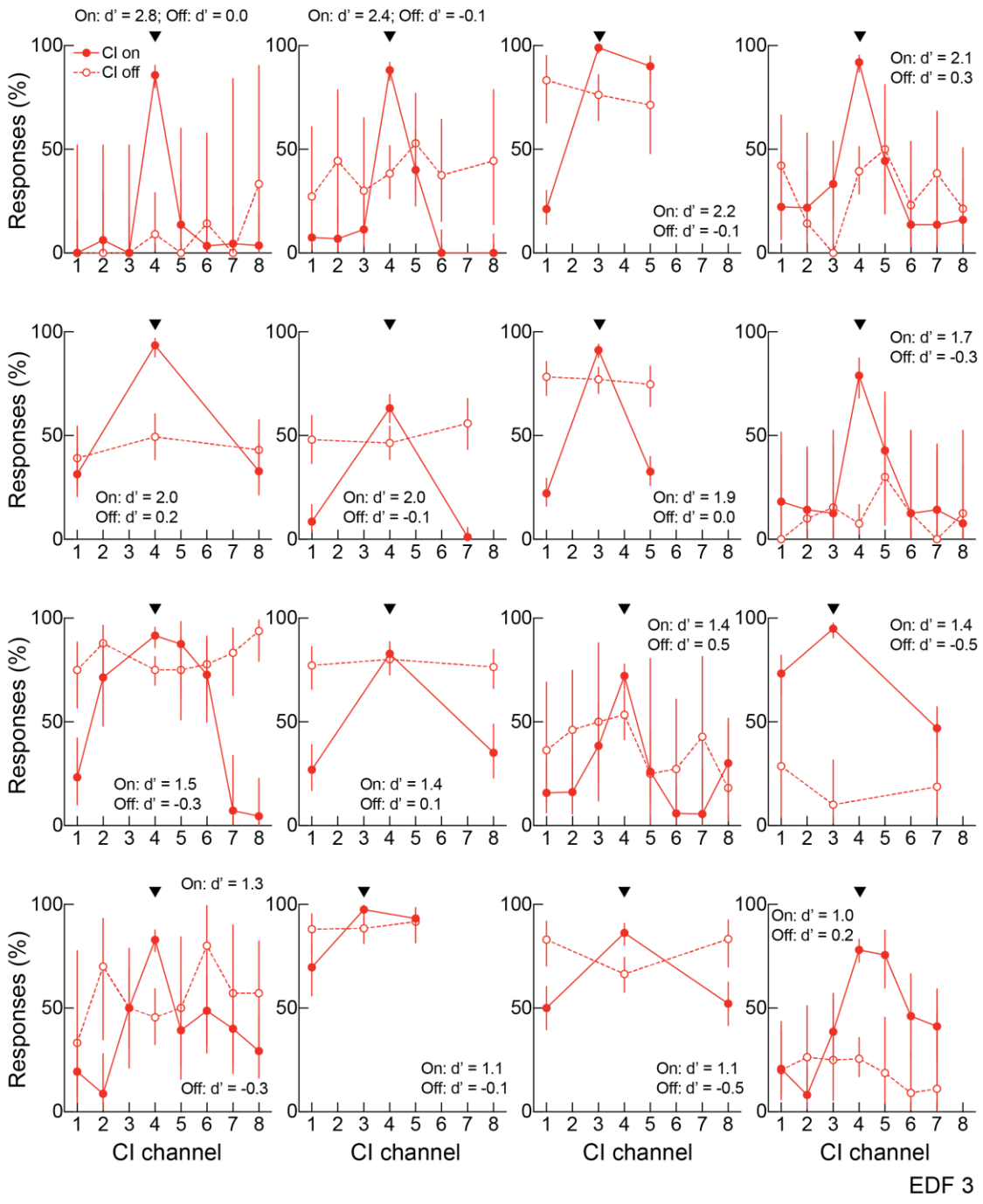
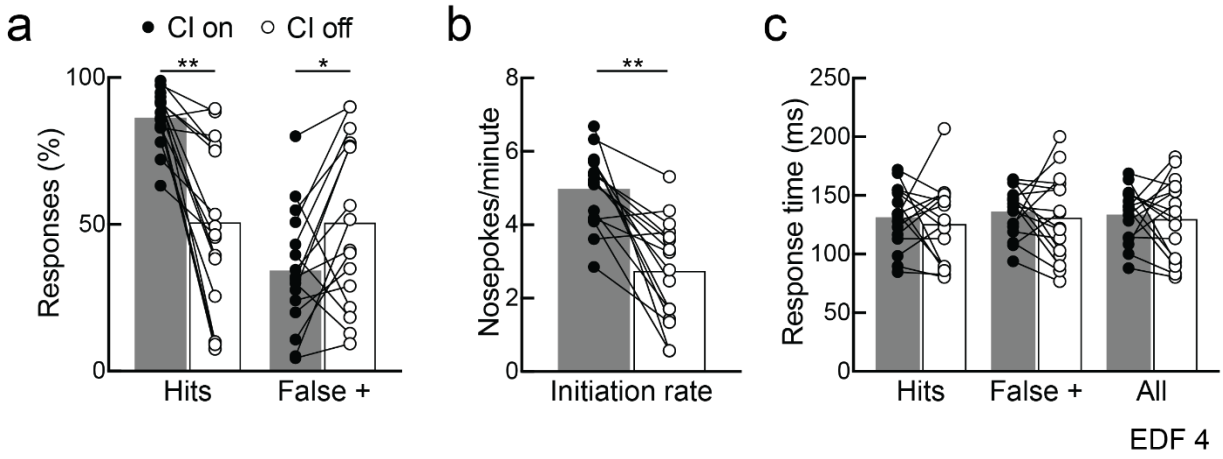
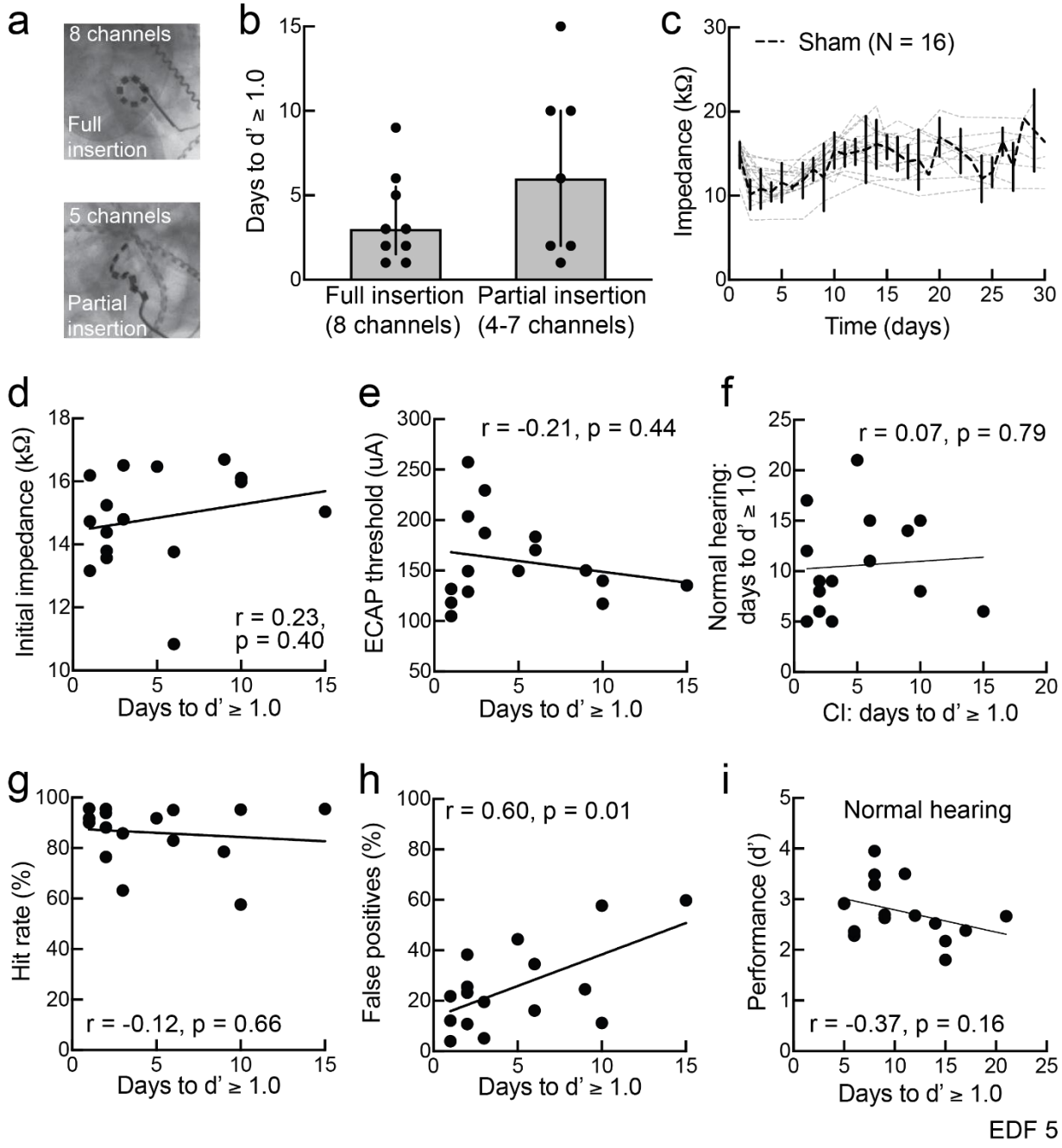
Extended Data Figure 2. Cochlear implant programming. a, Depiction of center frequencies for individual cochlear implant channels. **b,** Frequency allocation tables used to select tones for behavioral conditioning based on the center frequency of channels with different electrode configurations. **c,** Example electrodograms, showing that only the cochlear implant channel for selected center frequency was activated by the tone.



Extended Data Figure 3. Deafened animals used the cochlear implant to perform the auditory task. Response rates across cochlear implant channels for all 16 rats from **Figure 1** with the cochlear implant turned on (filled circles) or turned off (open circles). Arrowhead, target tone programmed to activate channel 3 or 4. Error bars, 95% confidence interval.

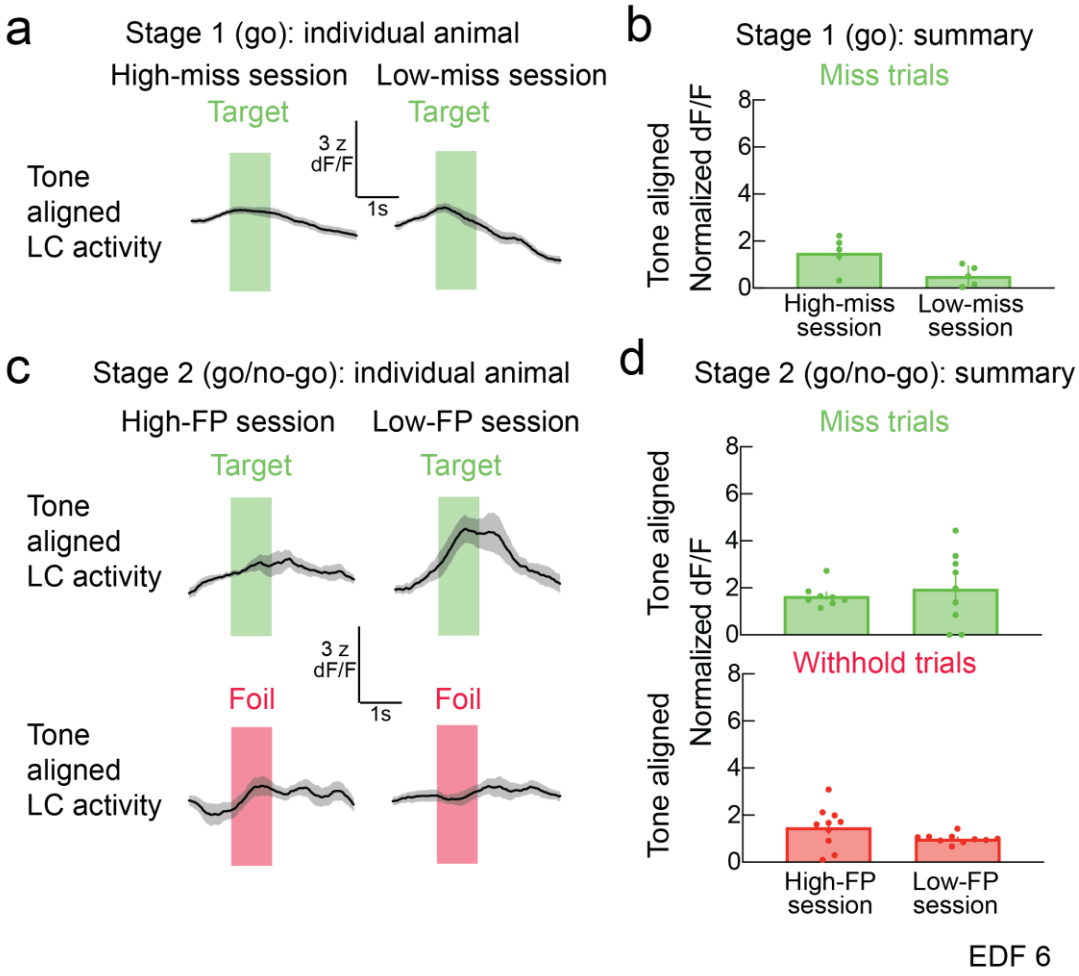


Extended Data Figure 4. Deafened animals were unable to perform the auditory task without cochlear implant input. a, Hit rates were lower and false positives were higher in rats when the cochlear implant was off (N = 16, on vs off, hits: $p = 0.0001$; false positives: $p = 0.02$; paired two-tailed Student's t-tests). **b,** Initiation rates decreased when the cochlear implant was turned off (on vs off, $p < 0.0001$; paired two-tailed Student's t-test). **c,** Response times were similar across trial types, whether the cochlear implant was on or off (on vs off, hits: $p = 0.58$; false positives: $p = 0.59$; all: $p = 0.70$; paired two-tailed Student's t-tests). *, $p < 0.05$; **, $p < 0.01$.

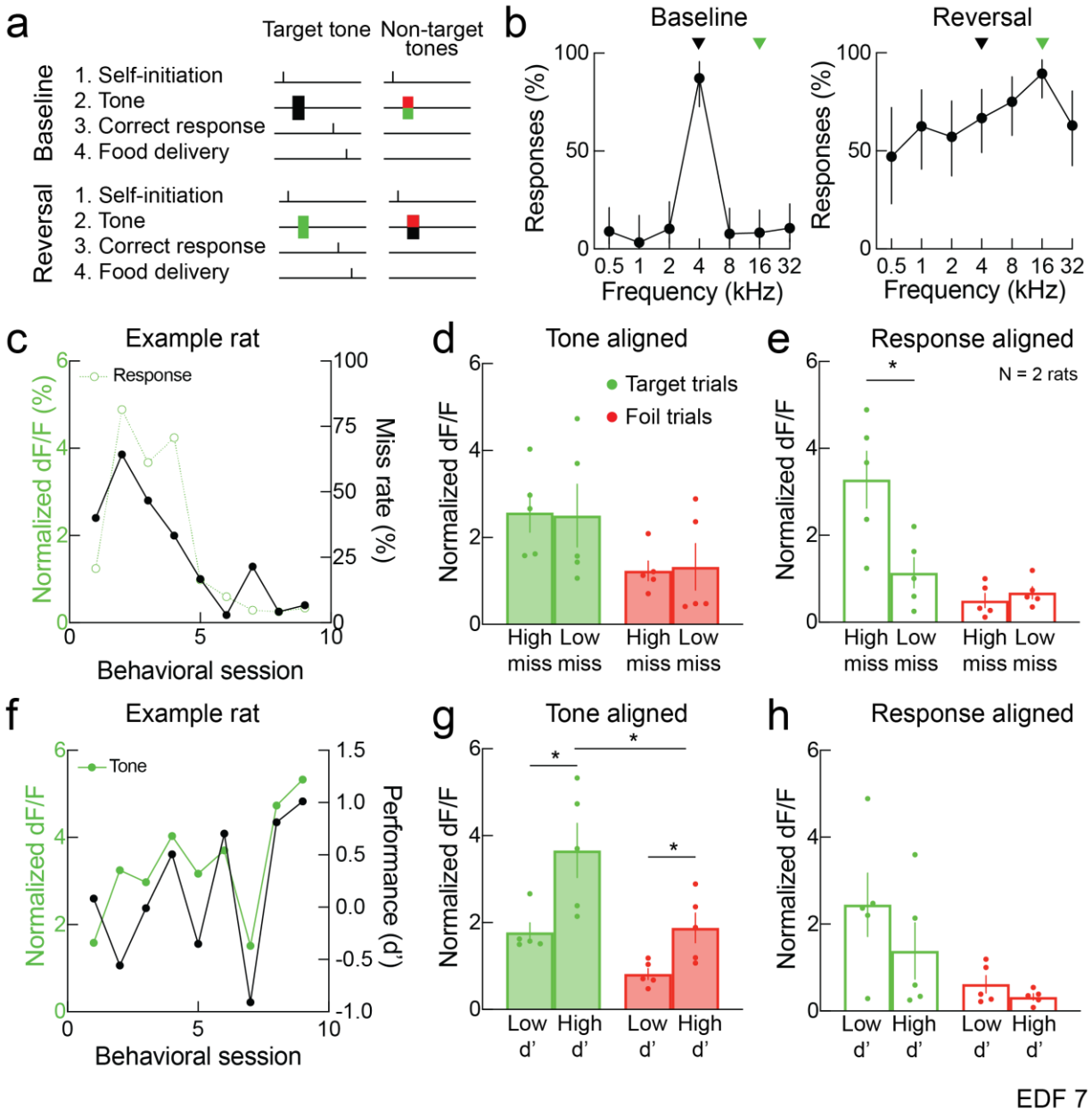


Extended Data Figure 5. Individual variability with implant use was related to false positive rate but not insertion depth, impedance, ECAP thresholds, hit rates, or normal-hearing performance. a, Example x-rays of full insertion (8 channels) and partial insertion (4-7 channels). **b,** Days to d' ≥ 1.0 did not differ based on cochlear implant insertion depth (full insertion vs partial

insertion, p = 0.32, unpaired two-tailed Mann–Whitney test). Median ± interquartile range. **c,** Average impedance of active cochlear implant channels over time. Grey dashed lines, individual rats. Black, mean ± s.e.m. **d,** Days to d' ≥ 1.0 did not correlate with initial impedance values (N = 16, Pearson's r = 0.23, p = 0.40). **e,** Days to d' ≥ 1.0 did not correlate with ECAP threshold (Pearson's r = -0.21, p = 0.44). **f,** Cochlear implant learning days to d' ≥ 1.0 did not correlate normal-hearing learning days to d' ≥ 1.0 (Pearson's r = 0.07, p = 0.79). **g,** Days to d' ≥ 1.0 did not correlate with hit rate (Pearson's r = 0.16, p = 0.56). **h,** Days to d' ≥ 1.0 correlated with false positives (Pearson's r = 0.61, p = 0.01). **i,** During normal-hearing training, days to d' ≥ 1.0 did not correlate with maximum d' performance (Pearson's r = -0.37, p = 0.16).

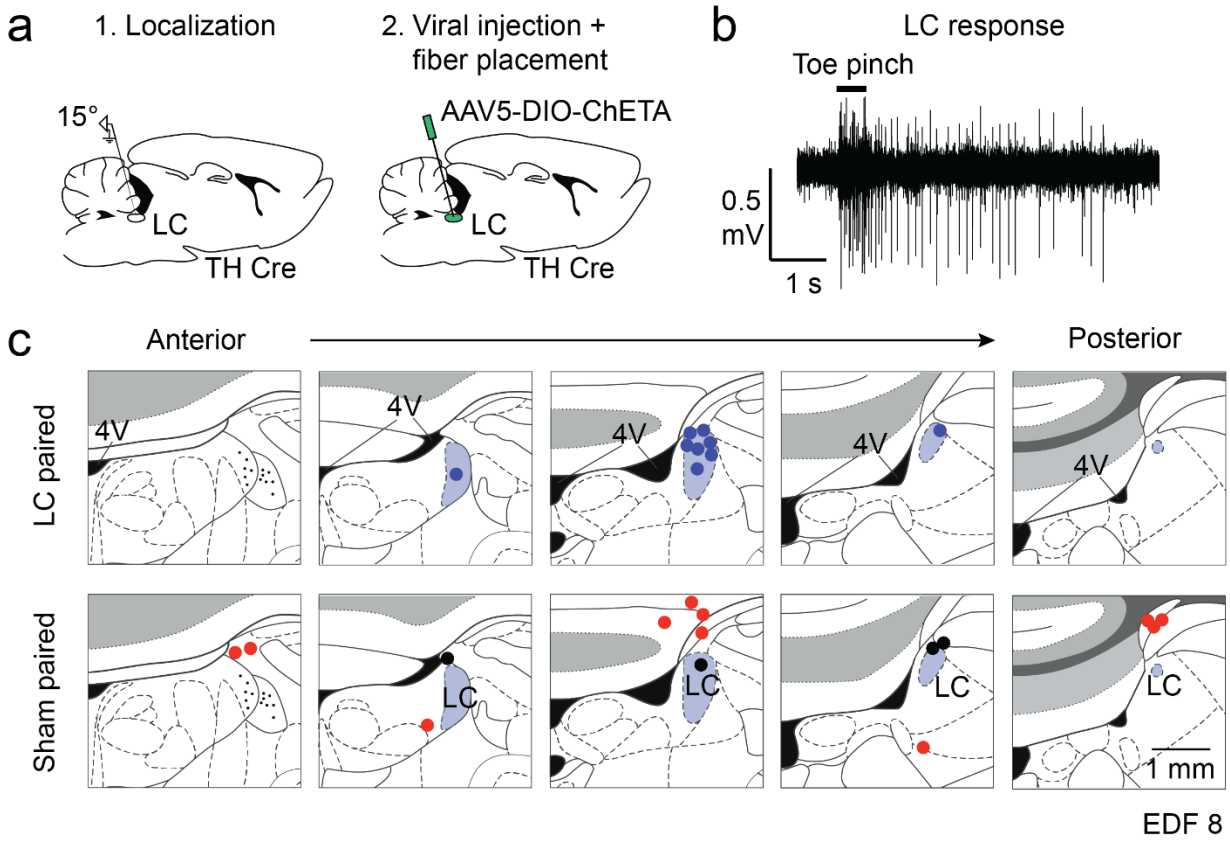


Extended Data Figure 6. Fiber photometry miss/withhold analysis. a, Example locus coeruleus (LC) activity aligned to tone onset during stage one training with cochlear implant, showing trial-averaged misses in an early high-miss rate behavioral session (left) and in a later low-miss behavioral session (right). **b,** Tone-aligned normalized dF/F locus coeruleus signals in high-miss and low-miss behavioral sessions. **c,** Example locus coeruleus activity aligned to tone onset during stage two (foil and target training). Miss and withhold trials in a high-false positive (FP) behavioral session (left). Miss and withhold trials in a low-FP behavioral session (right). **d,** Tone-aligned normalized dF/F locus coeruleus signals during miss trials and withhold trials in high-FP and low-FP behavioral sessions. Data are mean ± s.e.m.

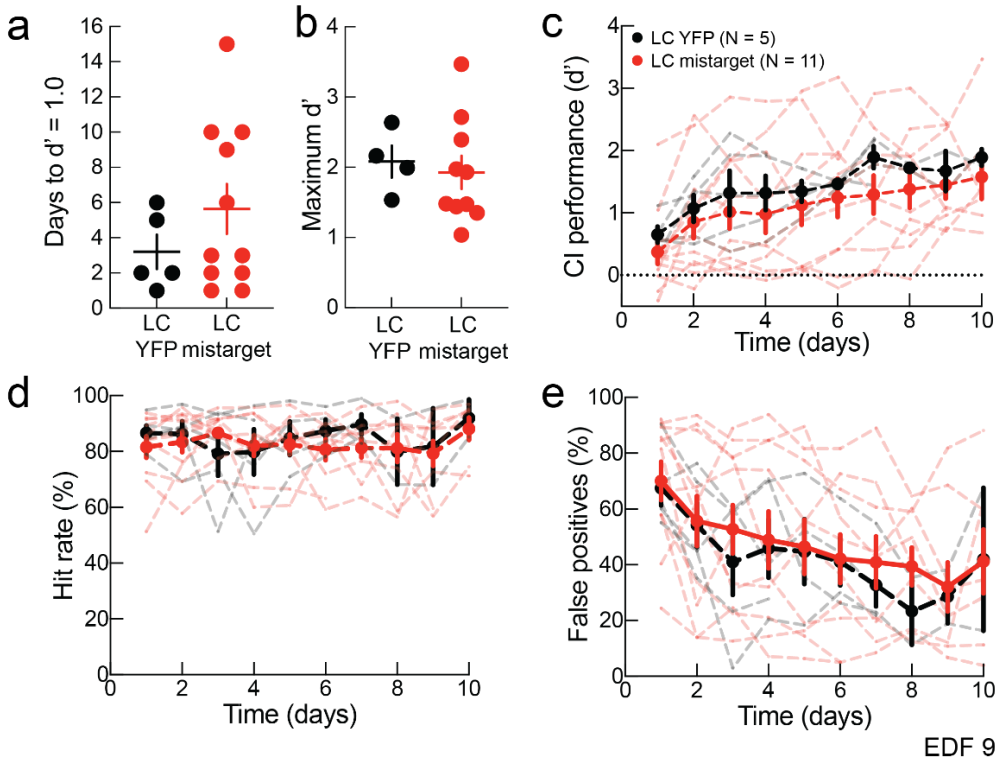


Extended Data Figure 7. Locus coeruleus activity in normal-hearing reversal learning. a, Schematic of go/no-go auditory behavioral task in normal-hearing rats when target tone is changed to a different frequency. After training to response to one target tone (black) while withholding from foil tones (green/red), one of the previously unrewarded tones (green) became the rewarded tone and the previously rewarded tone (black) became unrewarded. **b,** Example of animal

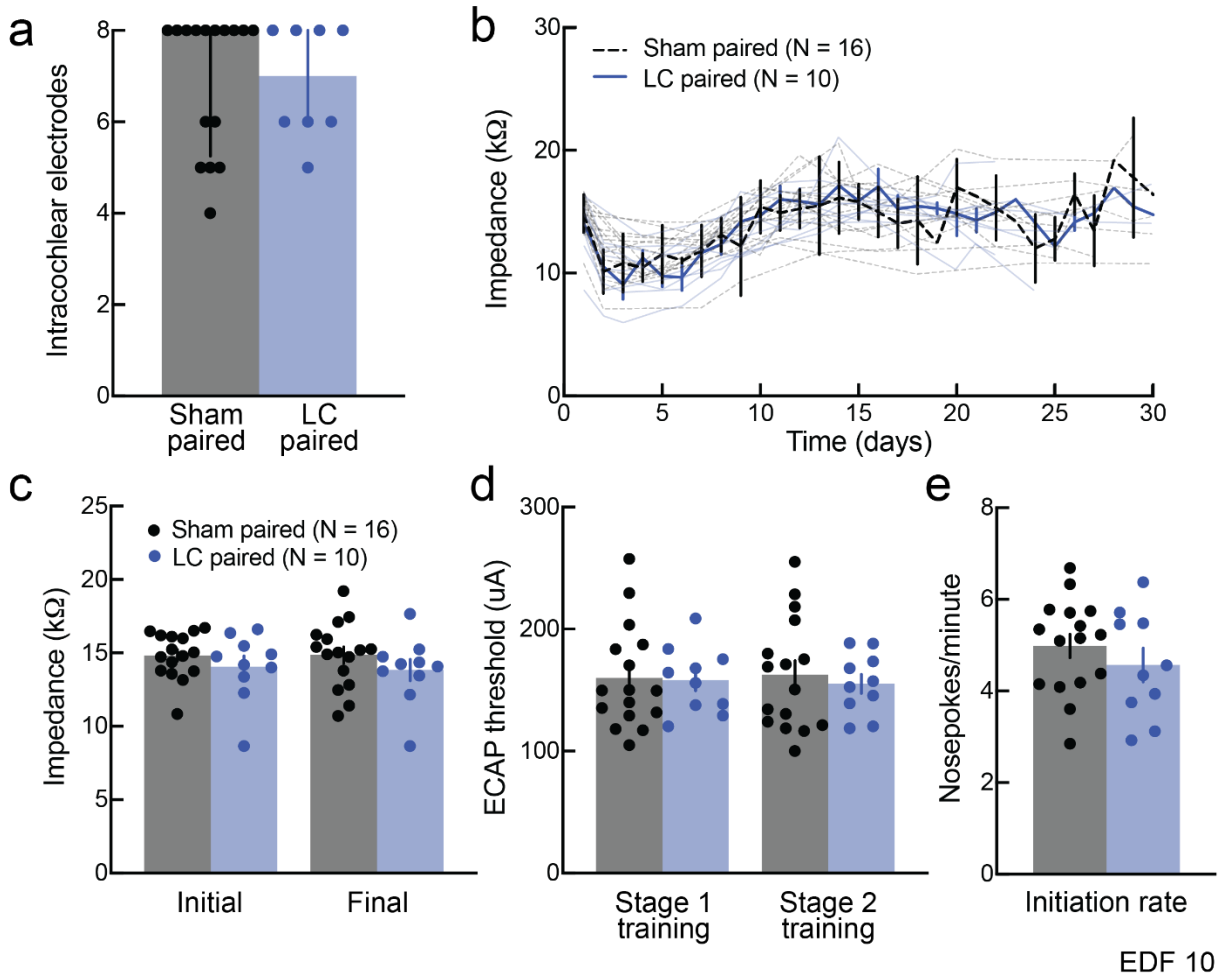
performance on this task to first and second rewarded tones. Black arrowhead, first rewarded tone; green arrowhead, second rewarded tone. Error bars, 95% confidence intervals. **c**, Example of response-aligned locus coeruleus activity and miss rates across time. **d,** Tone-aligned normalized dF/F in locus coeruleus was similar across miss rate sessions on hit target trials ($p = 0.93$, unpaired two-tailed Student's t-test) and false positive foil trials ($p = 0.88$, unpaired two-tailed Student's t-test). **e,** Response-aligned normalized dF/F in locus coeruleus was higher on target hit trials in high-miss sessions ($p = 0.02$, unpaired two-tailed Student's t-test), but comparable across miss rates for false positive foil trials ($p = 0.43$, unpaired two-tailed Student's t-test). **f,** Example tone-aligned locus coeruleus activity and performance (d') across time. **g,** Tone-aligned normalized dF/F in locus coeruleus was higher when d' was high on hit target trials ($p = 0.02$, two-tailed unpaired Student's t-test), as well as on false positive foil trials ($p = 0.02$, unpaired two-tailed Student's t-test), but higher on hit trials than on foil trials ($p = 0.04$, unpaired two-tailed Student's t-test). **h,** Response-aligned normalized dF/F in locus coeruleus was similar across d' values on target hit trials ($p = 0.31$, unpaired two-tailed Student's t-test) and for false positive foil trials ($p = 0.21$, unpaired two-tailed Student's t-test). Data are mean ± s.e.m. *, $p < 0.05$.



Extended Data Figure 8. Locus coeruleus targeting. a, Surgical approach for targeting locus coeruleus. Multi-unit recordings were conducted to locate locus coeruleus (LC) and then viral injection and optic fiber placement were based on these coordinates. **b,** Example multi-unit activity in locus coeruleus evoked by toe pinch. **c,** Optical fiber placement based on histology and CT/MRI co-registration. Top, fiber placement in locus coeruleus paired animals. Bottom, fiber placement in sham animals (red, mistargeted fibers outside of locus coeruleus; black, YFP-injected controls). Scale bar, 1 mm.



Extended Data Figure 9. Cochlear implant performance was comparable between sham paired YFP-injected animals vs fiber-mistargeted animals. a, Days to d' ≥ 1.0 was similar between the two sub-groups of sham animals with either YFP-only expression in locus coeruleus (LC) or when fiber was mistargeted outside of locus coeruleus (YFP: N = 5 rats, mistargeted: N = 11 rats, p = 0.38, unpaired two-tailed Mann–Whitney test). Median ± interquartile range. **b,** Sham animals in each subgroup with at least six days of cochlear implant training had similar maximum d' (YFP: N = 4 rats vs, mistargeted: N = 10 rats, p = 0.71, unpaired two-tailed Student's t-test). **c,** Implant performance (d') over time in YFP vs mistargeted animals. One YFP animal and one mistargeted animal shown in **a,c** each did not reach the six-day requirement for maximum performance analysis; these animals are not displayed in **b**. **d,** Hit rates. **e,** False positives. Data are error bars, mean ± s.e.m. except in **a**.



Extended Data Figure 10. Locus coeruleus vs sham paired animals had comparable implant insertions, impedances, ECAPs, behavioral initiation rates, and lack of residual hearing. a, Number of intracochlear electrodes as assessed by x-ray was similar between locus coeruleus (LC) paired rats and sham paired rats (locus coeruleus paired, N = 10 rats vs sham paired, N = 16 rats, p = 0.93, unpaired two-tailed Mann–Whitney test). Error bars, median ± interquartile range. **b,** Average impedances of cochlear implant channels over time in locus coeruleus paired vs sham paired rats. **c,** Both initial and final impedance values were similar in locus coeruleus paired and sham paired rat (locus coeruleus paired vs sham paired, initial: p = 0.32; final: p = 0.27; unpaired two-tailed Student's t-test). **d,** ECAP thresholds during stage one and stage two training did not

differ between locus coeruleus paired and sham paired rats (locus coeruleus paired vs sham paired, stage one: $p = 0.91$; stage two: $p = 0.64$; unpaired two-tailed Student's t-test). **e,** Initiation rates were similar between locus coeruleus paired and sham paired rats (locus coeruleus paired vs sham paired, $p = 0.35$; unpaired two-tailed Student's t-test). Data are error bars, mean ± s.e.m. except in **a**.