

AUDITORY EXPERIENCE WITH BILATERAL COCHLEAR IMPLANTS SHAPES INTERAURAL TIME DIFFERENCE TUNING

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Introduction

- Sound localization relies on binaural cues such as **interaural time differences (ITDs)**, which refers to the **difference in sound arrival time between the two ears**.
- **Cochlear implants (CIs)** are the most successful neural prosthesis worldwide, yet sound localization remains challenging for **bilateral CI users**, largely due to **reduced sensitivity to ITDs** [1].
- **Under optimized stimulation conditions** providing temporally accurate binaural cues, even the **neonatally deafened auditory system can exhibit ITD sensitivity** [2].
- It is **unknown** how **optimized stimulation conditions** alter **neural tuning in the auditory midbrain**.

Research question:

Does optimized ITD lateralization training via bilateral CIs change the auditory midbrain tuning in rats without hearing experience?

Methods: CI implantation and electrophysiological measurements

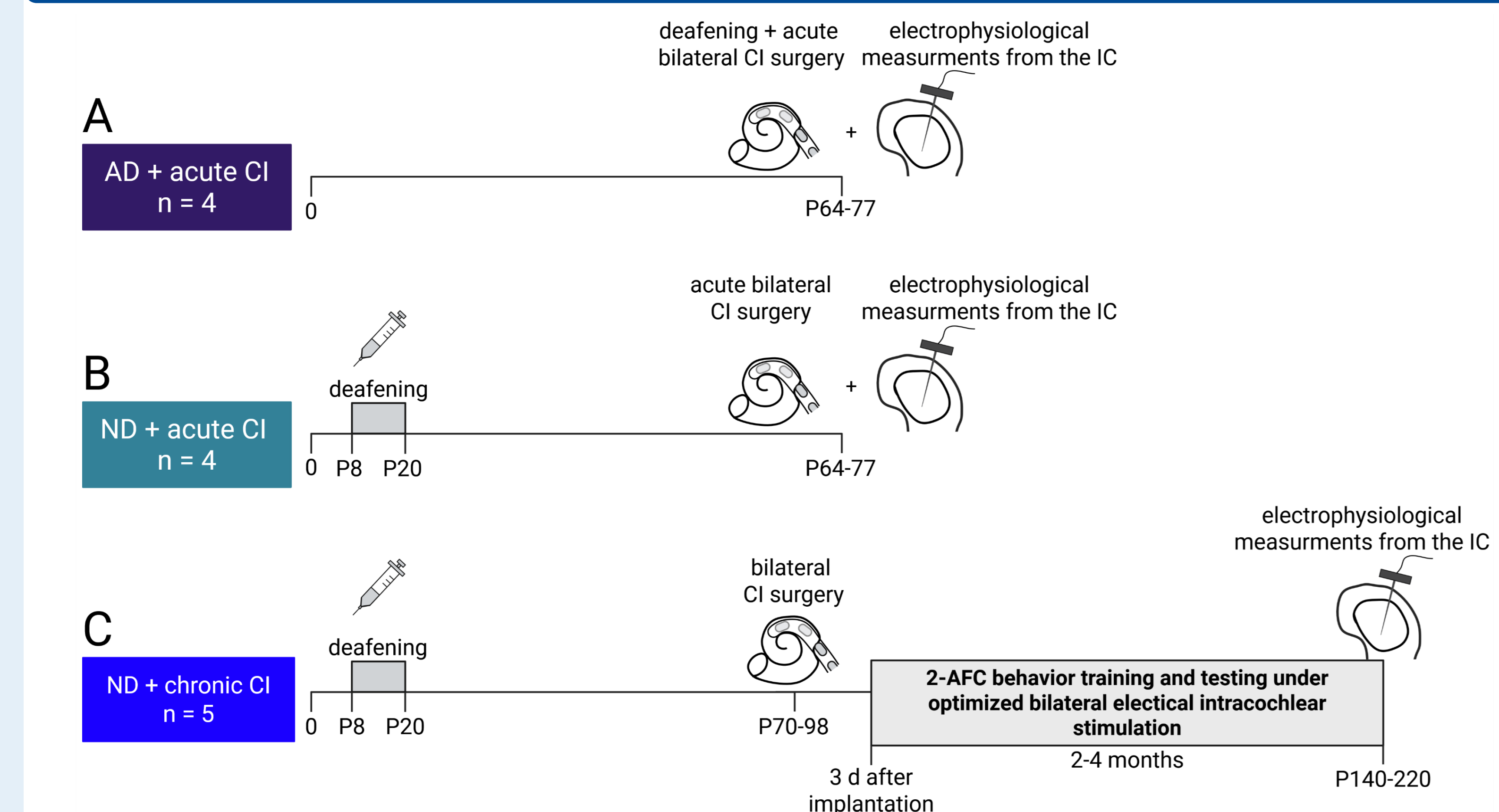


Figure 1: Experimental timetable for the three different cohorts. (A) Four animals were adultly deafened (AD) and acutely bilaterally implanted with CIs immediately prior to neurophysiological recordings from the inferior colliculus (IC). (B) Four neonatally deafened (ND) rats were acutely supplied with CIs before recordings from IC. Data from cohort (A) and (B) has previously been published in Buck et al. 2021 [3]. (C) Five ND rats were bilaterally supplied with CIs in young adulthood. These animals underwent behavioral training in a 2-alternative forced choice tasks (2-AFC) and electrophysiological recordings afterwards.

- **Neurophysiological recordings (Fig. 2):**
 - Recording electrode: ATLAS Neuroengineering, E32-50-S1-L10
 - Recording area: Inferior colliculus (IC)
 - CI stimulation: ITDs $\pm\{0, 40, 80, 120\}$ μ s
 - Pulse rate: 1 Hz

Data analysis:

For each stimulus and for each channel the analog multi-unit activity (AMUA; [4]) was calculated.

ITD tuning curves for each multi-unit were normalized (z-score) and in total 3488 multi-units were clustered via principal component analysis (PCA; Fig. 3 and 4).

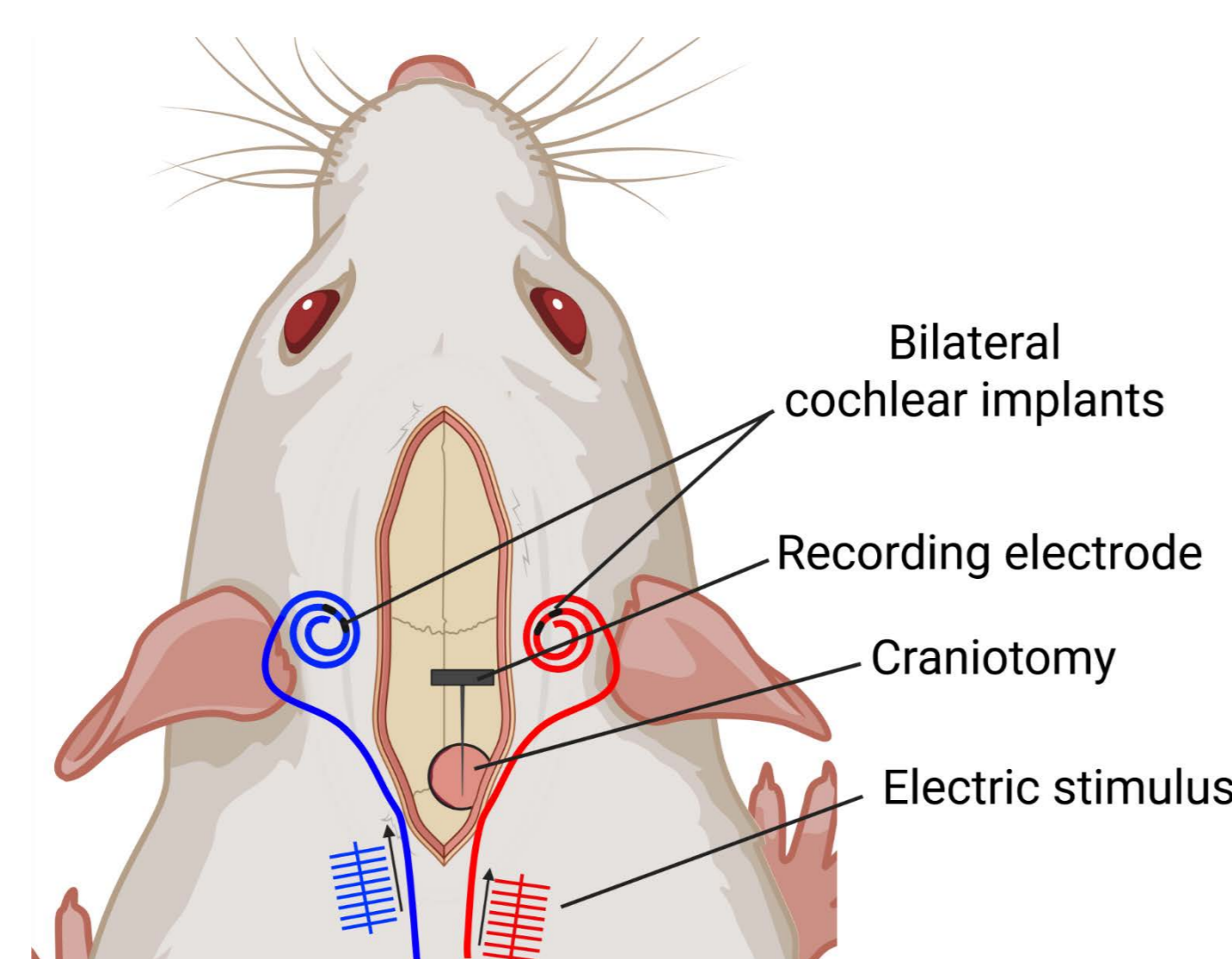


Figure 2: Cartoon illustrating the experiment. Rats were bilaterally implanted with CIs via cochleostomy and a recording electrode array was inserted into the IC. Created with Biorender.com

Results I: Sample tuning curves of IC neurons

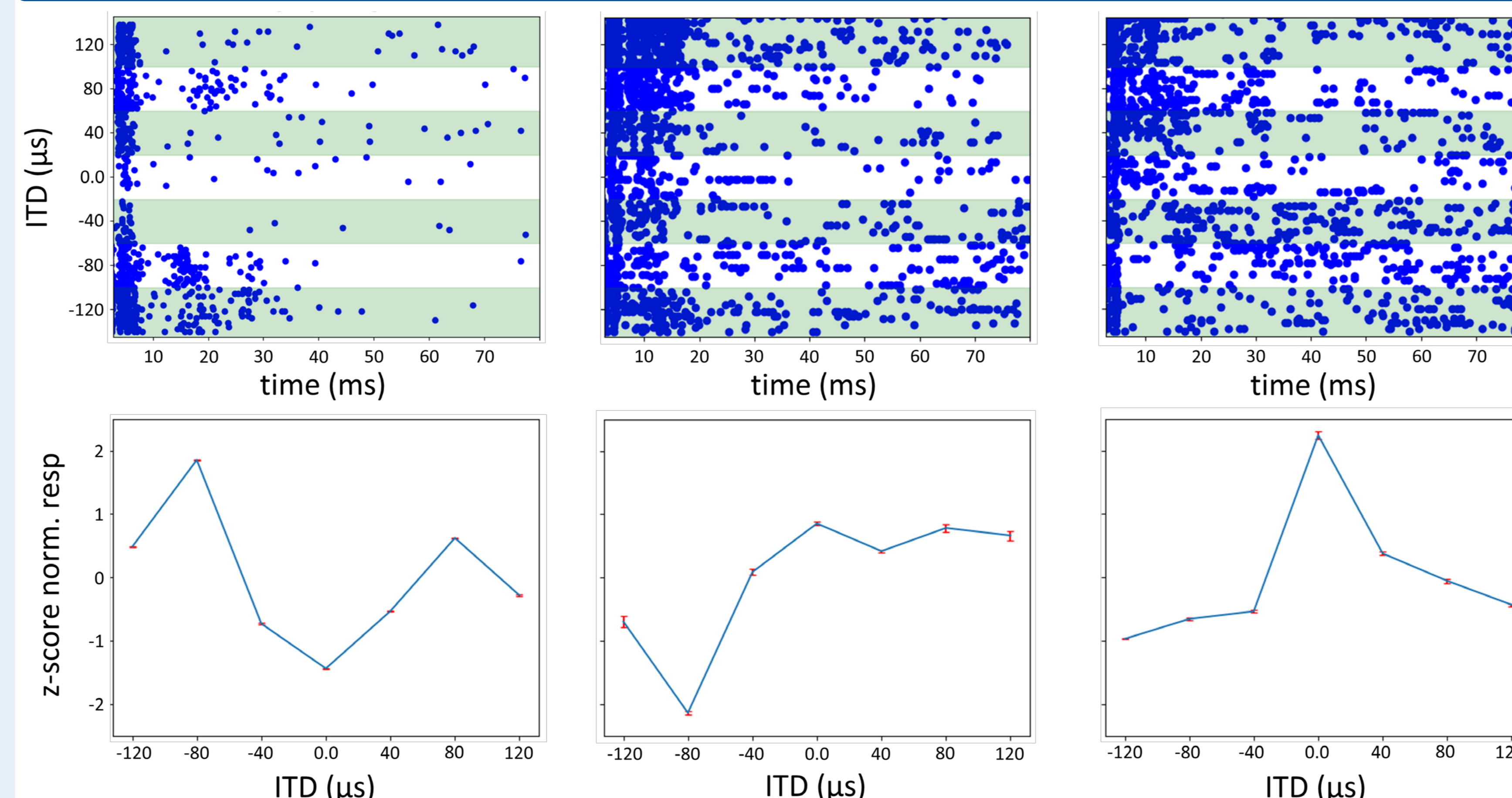


Figure 3: Spike raster plots and tuning curves for representative sample multi-units of IC. Upper row: each blue dot represents a spike, determined by simple threshold crossing algorithm. Responses for different ITD values are indicated by the alternating white and light green backgrounds. Bottom row: corresponding AMUA tuning curves for the seven presented ITDs. AMUA responses were z-score normalized. Error bars indicate the standard error of the mean. Negative values represent contralateral ITDs while positive values represent ipsilateral ITDs.

Results II: Clustering of neural tuning curves

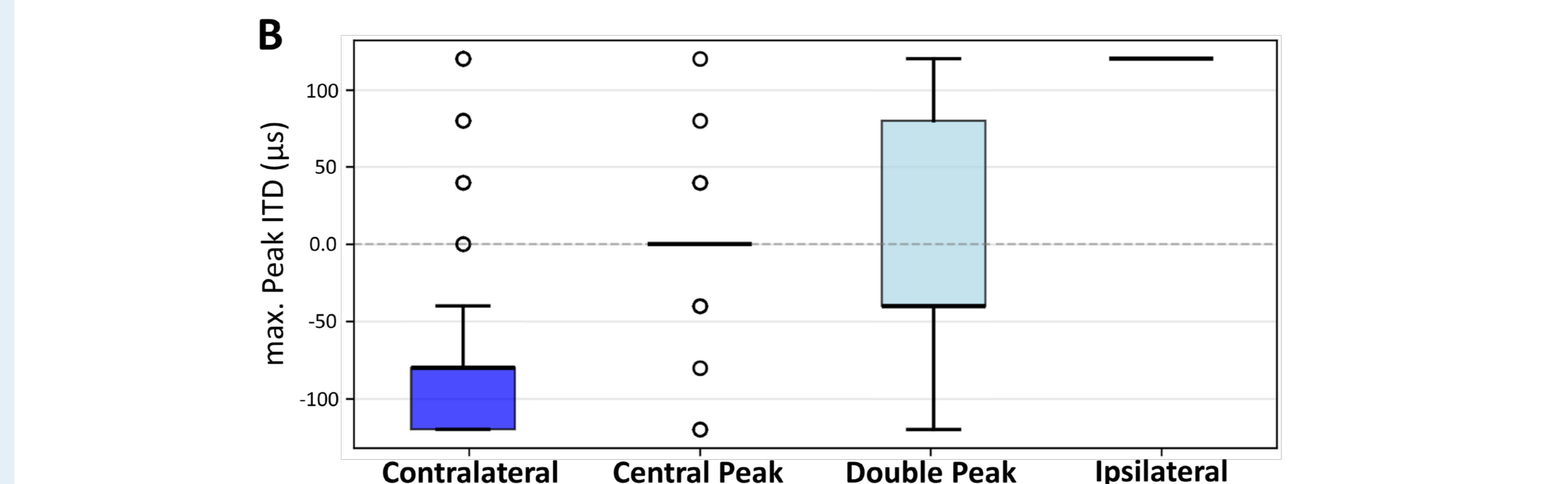
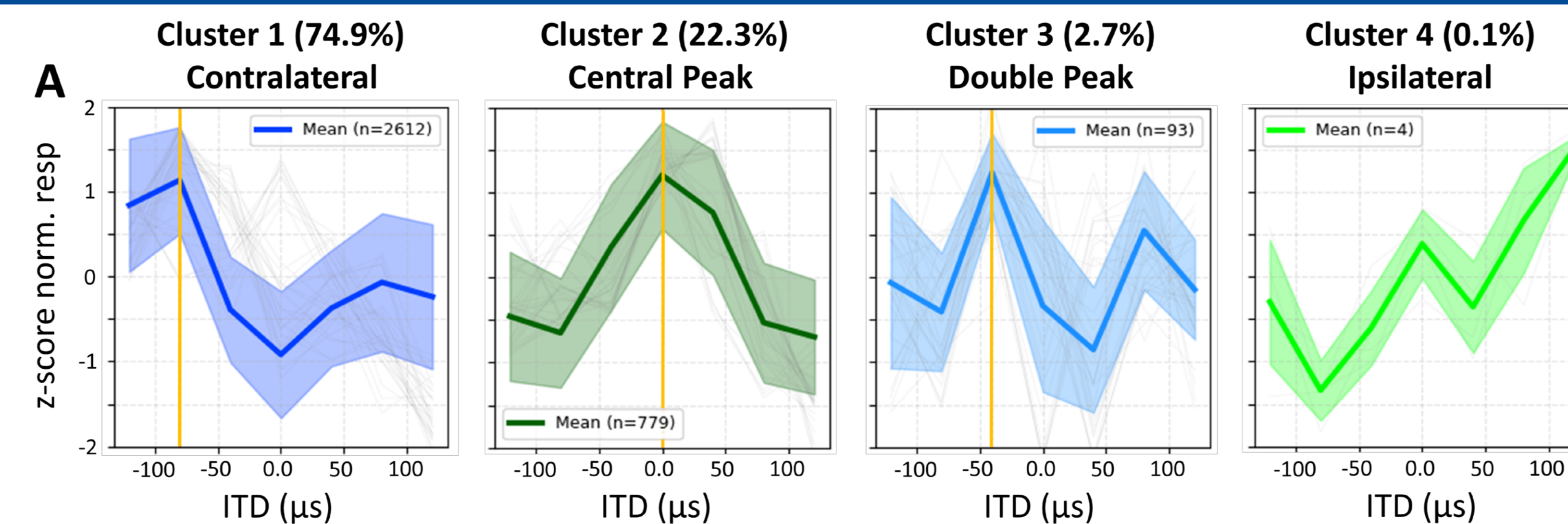


Figure 4: Clustering ITD tuning curves. (A) The four most prominent ITD tuning curve clusters defined by PCA. ITD tuning curves were z-score normalized previous to clustering. The percentage of units in each cluster decreases from left to right (see sub headers). Shading depicts the standard deviation. Vertical orange line indicates the peak ITD in each plot. (B) Distribution of maximum peak ITDs of all units in a respective cluster in μ s. In total 3488 multi-units, recorded from the three cohorts, were clustered.

Results III: Proportion of neural tuning curves by cohort and animal

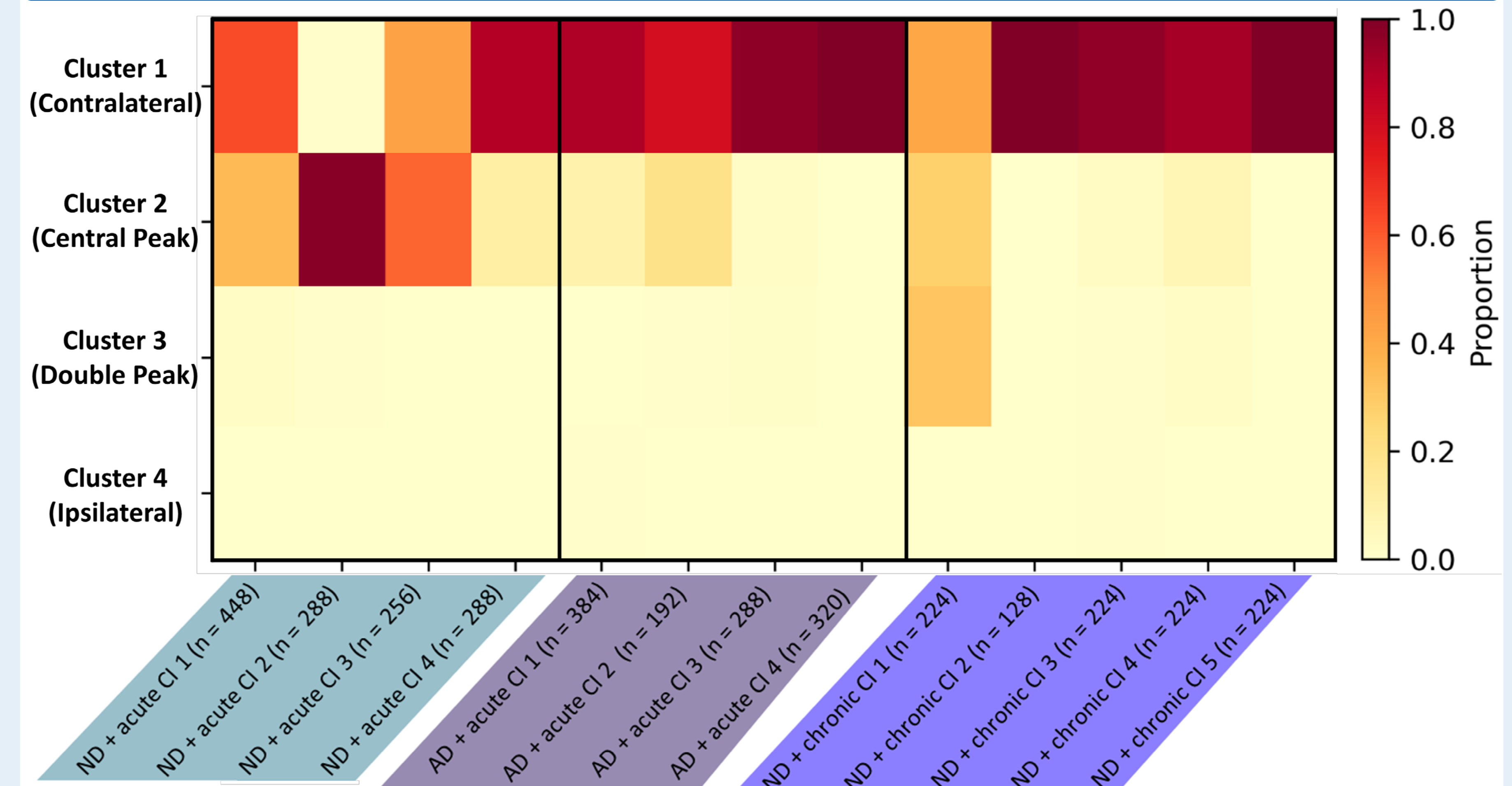


Figure 5: Cluster distribution per cohort and animal. The four left most columns depict the ND + acute CI cohort (B in Fig. 1). The tuning curves of this cohort are mainly **contralaterally** and **centrally** tuned. The tuning curves of the AD + acute CI cohort are mainly **contralaterally** tuned. The ND + chronic CI rats (C in Fig. 1) that were trained and tested on their ITD sensitivity after CI implantation show similar tuning curve distributions as the AD + acute CI cohort and are mainly **contralaterally** tuned. Proportion of these clusters for each animal is presented by color scale (right axis) and the respective number of units per animal is written in the x-axis label.

- The tuning curves of the ND + acute CI cohort are divided almost equally between **contralaterally** and **centrally** tuned (Fig. 5).
- The centrally tuned cluster with a peak at 0 μ s ITD mainly consist of tuning curves from the ND + acute CI cohort (Fig. 4 and 5).
- The ITD tuning curves of the four AD + acute CI animals are mainly **contralaterally** tuned (Fig. 4 and 5).
- The chronically CI implanted animals have a tuning curve distribution similar to that of the AD + acute CI cohort.

Conclusions

- ITD sensitivity is present even in the neonatally deafened, hearing inexperienced auditory system.
- However, the hearing inexperienced auditory system shows a reduced dominance of the normal hearing like contralateral ITD tuning pattern.
- Using optimized binaural CI stimulation, the early deafened auditory experience can re-establish a normal hearing like contralateral ITD tuning.

References:

- [1] Litovsky, R. Y. and Gordon, K. (2016). Bilateral cochlear implants in children: Effects of auditory experience and deprivation on auditory perception, *Hear. Res.* 338 : 76-87
- [2] Rosskoth-Kuhl, N.; Buck, A. N.; Li, K. and Schnupp, J. W. (2021). Microsecond interaural time difference discrimination restored by cochlear implants after neonatal deafness, *eLife* 10: e59300
- [3] Buck A. N., Rosskoth-Kuhl N., Schnupp J. W. (2021). Sensitivity to Interaural Time Differences in the Inferior Colliculus of Cochlear Implanted Rats with or without Hearing Experience, *Hear. Res.* 408: 108305.
- [4] Schnupp J. W., Jose A. G., L. A. Nicholas, (2015). Periodotopy in the gerbil inferior colliculus: local clustering rather than a gradient map, *Front. Neural Circuits* 9.