Inter-collicular suppression compresses all types of rate-amplitude functions of inferior collicular neurons in mice

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Short title: Inter-collicular suppression on sound processing

Abstract

The two inferior colliculi (IC) are paired structures in the midbrain that are connected to each other by a bundle of commissural fibers. The fibers play an important role in coordinating sound signal processing between the two inferior colliculi. This study examined inter-collicular suppression on sound signal processing in amplitude domain of mice by measuring the rate-amplitude functions (RAFs) of neurons in one IC during the electrical stimulation of the opposite IC. Three types (monotonic, saturated and non-monotonic) RAFs of collicular neurons were measured before and during inter-collicular suppression. Inter-collicular suppression significantly increased the slope, decreased the dynamic range and narrowed down the responsive amplitude of all RAFs to high amplitude level but did not change the type of most (36/43, 84%) RAFs. As a result, all types of RAFs were compressed at a greater degree at low than at high sound amplitude during inter-collicular suppression. These data indicate that inter-collicular suppression improve sound processing in the high amplitude domain.

Key words: inter-collicular suppression; rate-amplitude function; amplitude-coding; inferior colliculus

1. Introduction

The inferior colliculi (IC) are paired mammalian structures in the midbrain that receive excitatory and inhibitory ascending and descending projections and are also connected to each other by a bundle of fibers called the commissure of IC (CoIC) (Aitkin and Phillips 1984, Syka and Popelář, 1984, Herrera *et al*. 1987, Oliver *et al*. 1991, Saldana and Merchan 1992, Malmierca *et al*. 1995, 2009, Moore *et al*. 1997, Popelář *et al*. 2003, Cant and Benson 2006, Hernández *et al*. 2006, Winer 2006). CoIC fibers include point-to-point connections between the corresponding frequency laminae of the two ICs as well as divergent connections projecting from one IC neuron to a wide range of frequency laminae in the opposite IC (Malmierca *et al*. 1995, 2009). These connections provide the final opportunity for functional interactions between the two sides of the auditory pathway at the subcortical level.

In vitro studies have demonstrated that microelectrical stimulation (ES) of CoIC fibers elicits both excitatory and inhibitory postsynaptic potentials (EPSPs and IPSPs, respectively) in IC neurons (Smith 1992, Moore *et al*. 1998). Similarly, blocking CoIC fibers *in vivo* by injecting kynurenic acid (a nonspecific glutamatergic antagonist) into one IC changes the number of impulses and the frequency-response area of neurons located in the corresponding frequency laminae of the opposite IC (Malmierca *et al*. 2003, 2005, Orton and Rees 2014). Such inter-collicular interactions through CoIC provide opportunity for modulation during ascending auditory processing in multiple parametric domains including frequency and amplitude (Mei *et al*. 2012a, b, 2013, Cheng *et al*. 2013). In amplitude domain, inter-collicular interactions modulate the response magnitude and the rate-amplitude function

(RAF) of collicular neurons and changes the minimal threshold (MT) and dynamic range (DR) through the interplay between focused facilitation and widespread suppression in the CoIC (Mei *et al*. 2012a). Widespread inter-collicular suppression increases the sensitivity of IC neurons to minor changes over a narrower range of sound amplitude while focused facilitation produces the opposite effect (Mei *et al*. 2012b).

To further study the inter-collicular interaction on sound processing in amplitude domain, we examine the effect of electrical stimulation of one IC on the RAF of the neurons in the other IC. Specifically, we examine if the degree of inter-collicular suppression during electrical stimulation of one IC may vary with the type of affected collicular neurons in the other IC.

2. Methods

All experiments were approved by the Institutional Animal Care and Use Committee of Central China Normal University and complied with the Guide for the Care and Use of Laboratory Animals (NIH Publication No. 85-23, revised 1996).

2.1 Animal preparation and surgery

As described in our previous studies (Mei *et al*. 2012a, Cheng *et al*. 2013), a flat head of a 1.8 cm nail was glued onto the exposed skull of each of 21 Nembutal-anesthetized (60–90 mg / kg b. wt.) Kunming mice (*Mus musculus*, Km, 20–25 g, b. wt.) with acrylic glue and dental cement. After securing the mouse to an aluminum plate with a plastic band inside a sound-proof room (at a temperature of 28–30 ºC), its head was immobilized by a set of screw.

Small holes (diameter: 200–500 µm) were made in the skull above each IC. A 2 M NaCl glass pipette electrode (tip diameter: <1 µm, impedance: 5–10 MΩ) was orthogonally inserted into one IC to record sound activated responses while a pair of custom-made bipolar tungsten electrodes (see below) was inserted into the other IC for focal electrical stimulation (ES) and recording sound activated responses of stimulated IC neuron.

2.2 Stimulation and isolation of acoustically evoked collicular (IC) neurons

For acoustic stimulation (AS), continuous sine sound waves from a function generator (GFG-8016G, Good Will Inst Co., Ltd, Bayan Lepas, Penang, Malaysia) were formed into 40 ms pure tone (5 ms rise-decay times) with custom-made tone burst generator (electronic switch) driven by a stimulator (Model SEN-7203, Nihon Kohden Co, Shinjuku, Tokyo, Japan). The tone pulses were then amplified (custom-made amplifier) after passing a decade attenuator (LAT-45, Leader, Kohokuku, Yokohama, Japan) before they were fed into a small loudspeaker (AKG model CK 50, 1.5 cm in diameter, 1.2 g, frequency response 1–100 kHz). The loudspeaker was placed 30 cm away from the mouse ear and 60° contralateral to the recording site. Calibration of the loudspeaker was conducted with a 1/4 inch microphone (4939, B&K, Denmark) placed at the mouse's ear using a measuring amplifier (2610, B&K, Denmark). The output of the loudspeaker was expressed in decibel sound pressure level (dB SPL) in reference to 20 µPa root mean square. The maximal available sound amplitude ranged from 95 dB to 110 dB SPL between 10 and 80 kHz but dropped off sharply to 80 dB SPL at 100 kHz thereafter.

Two insulated tungsten electrodes (FHC Inc, Bodowin, ME, USA) were glued together (glue 502, inter-tip distance: ≤100 μm) to form a pair of custom-made tungsten electrodes. These electrodes were used for recording sound activated IC responses and for focal electrical stimulation in the IC stimulating site (4 ms train of four monophasic pluses of 0.1 ms with 0.9 ms pluse-gap at 2 trains/s, 5–50 μA) using stimulator (Model SEN-7203, Nihon Kohden Co, Shinjuku, Tokyo, Japan) and stimulus isolation unit (CSS-202J, Nihon Kohden Co, Tokyo, Japan).

Upon isolation of an IC neuron in stimulating side (abbreviated as IC_{ES} neuron) using a pair of custom-made tungsten electrodes with 40 ms pure tone at 2 pulses/s, its best frequency (BF) and MT were audio-visually determined by changing the frequency and sound amplitude. The sound frequency that elicited the neuron's response at the lowest amplitude was defined as the BF. The threshold at the BF was defined as the MT. At the MT, the neuron, on average, responded with 50% probability to BF pulses. Acoustically evoked responses of an IC neuron in the recording side (abbreviated as IC_{Rec} neuron) was then isolated with a 2 M NaCl glass electrodes. After determining the BF and MT of this IC_{Rec} neuron, its response to BF sound pulses delivered at 10 dB above the MT was recorded as a control response. The neuron's response was then monitored again during ES of the IC_{ES} neuron isolated before. The ES was delivered between 5 and 50 μA and at a randomly chosen inter-pulse interval (IPI, interval between AS and ES). The current level was gradually increased in order to find an IC_{Rec} neuron affected by the IC_{ES} ES and to observe the effect on response of the IC_{Rec} neuron under different current level. Then, the ES current was fixed at moderate level (25 μA, high enough and without too much diffusion, Jen and Zhou 2003) and the IPI was adjusted systematically to determine the optimal IPI during which the ES would produce maximal effect. If the percent decrease in number of impulses of IC_{Rec} neuron induced by focal ES didn't reach 30%, the IC_{Rec} neuron was abandoned. Otherwise it was regarded as a modulated IC_{Rec} neuron by inter-collicular suppression. At the optimal IPI, the RAF of IC_{Rec} neuron was then measured before and during ES in IC_{ES}. A RAF was measured with the neuron's number of impulses obtained at MT and 10 dB increments above the MT with 40 ms BF sound. The best amplitude (BA) was defined as the specific amplitude which elicited the maximum in the neuron's number of impulses for a specific frequency. The dynamic range (DR) of RAF was defined as the amplitude range from 10% below the maximum to 10% above the minimum in the neuron's number of impulses. The middle DR (mDR) was defined as the middle amplitude value of DR. The slope of a RAF was obtained by dividing the percent change in the neuron's number of impulses within the dynamic range by the dynamic range and expressed in %/dB.

2.3 Data collection and analysis

Recorded action potentials were amplified and sent to a computer for acquisition of post-stimulus-time histograms (PSTH) (bin width: 250 μs; sampling period: 150 ms) to 32 stimuli. The total number of impulses in each histogram was used to quantify the neuron's response under each stimulation condition.

The suppressive effect on the RAFs of an affected IC_{Rec} neuron during the focal electrical stimulation of the opposite IC (i.e., IC_{ES}) was determined by calculating the percent decrease in the control number of impulses of the IC_{Rec} neuron. All data processed and plotted using Sigma Plot 2000. They were then quantitatively examined and statistically compared using SPSS 13.0 (one-way and repeated measures ANOVA at $P<0.05$, Stuendt's *t*-test and paired *t*-test at $P<0.05$).

3. Results

The responses of 43 $\mathrm{IC}_{\mathrm{Rec}}$ neurons were recorded during sound stimulation and their responses were suppressed during focal electrical stimulation of the opposite $\mathrm{IC}_{\mathrm{ES}}$ (Fig. 1Ba vs. b). Recording depth ranged from 227 to 2003 μm (mean ± SD: 1083 ± 401 μm), the BFs from 5.5 to 27.6 kHz (14.2 ± 4.8 kHz), and the MTs from 15 to 87 dB SPL (54 ± 17 dB SPL). Focal ES did not appear to affect the normal acoustically evoked response properties of $\mathrm{IC}_{\mathrm{ES}}$ neurons, which recovered to the control level after ES ceased (Fig. 1Aa vs. b). The RAFs of 43 neurons can be described as three groups, monotonic, saturated and non-monotonic. In the monotonic group (n=19, 44.2%), the neuron's number of impulses monotonically increased with sound amplitude (Fig. 2A-2). In the saturated group (n=12, 27.9%), the neuron's number of impulses increased with sound amplitude up to a maximum point, but then leveled out and did not increase more than 25% at higher sound amplitudes (Fig. 2B-2). In the non-monotonic group (n=12, 27.9%), the neuron's number of impulses increased with sound amplitude up to a maximum point and then decreased more than 25% at higher amplitudes (Fig. 2C-2).

Figure 2A-1, B-1, and C-1 show the PSTHs of three representative $\mathrm{IC}_{\mathrm{Rec}}$ neurons obtained with BF sound delivered at 10 dB above each neuron's MT before and during ES. Figure 2A-2, B-2, and C-2 show the RAFs of these three neurons before and during $\mathrm{IC}_{\mathrm{ES}}$ ES. It is clear that the percent inter-collicular suppression in the number of impulses of affected $\mathrm{IC}_{\mathrm{Rec}}$ neurons typically decrease with stimulus amplitude progressively increased above the MT. At the very high stimulus amplitude, percent suppression in the number of impulses reached a plateau level for IC_{Rec} neurons with the monotonic and saturated RAFs (Fig. 2A-3, B-3, A-4, B-4). However, the percent suppression in the number of impulses further increased at still high sound amplitude for IC_{Rec} neurons with non-monotonic RAFs (Fig. 2C-3, C-4). We further studied the effect of inter-collicular suppression on these non-monotonic neurons by dividing the mean percent suppression in Fig. 2C-4 into two parts based on the stimulus amplitude at which the mean percent suppression reversed its decreasing trend (Malmierca *et al*. 2005): part one, with percent suppression obtained ≤20 dB above MT; part two, with percent suppression obtained ≥30 dB above MT (Fig 3). Statistical analysis showed that the mean percent suppression in the part one was greater than that in the part two ($P<0.001$, Student's *t*-test), suggesting inter-collicular suppression in the number of impulses of affected non-monotonic IC_{Rec} neurons was stronger at low than at high sound amplitude, similar to monotonic and saturated IC_{Rec} neurons.

To study the inter-collicular suppression on sound processing in amplitude domain, we examine if inter-collicular suppression during electrical stimulation of one IC may change the type of RAF of affected neurons in the other IC. Table 1 compares the type of RAF of these IC_{Rec} neurons before and during ES of the opposite IC_{ES}. It is clear that the RAF of most IC_{Rec} neurons remained unchanged during ES of the opposite IC_{ES}.

We further studied the effect of inter-collicular suppression on the RAF of affected IC_{Rec} neurons in one IC by comparing the MT, BA, DR, mDR and slope of their RAF before and during electrical stimulation of the opposite IC_{ES}. Regardless of the type of the RAF of affected IC_{Rec} neurons, focal electrical stimulation of the IC_{ES} elevated the MT (Fig. 4A-1, B-1, C-1, $P<0.001$, Student's paired *t*-test), decreased the DR (Fig. 4A-3, B-3, C-3, $P<0.001$, Student's paired *t*-test), shifted the mDR toward a high-stimulus amplitude (Fig. 4A-4, B-4, C-4, $P<0.01-0.001$, Student's paired *t*-test), and increased the slope (Fig. 4A-5, B-5, C-5, $P<0.05-0.01$, Student's paired *t*-test) of the RAF of the IC_{Rec} neurons. There was no significant different in the degree of inter-collicular suppression effect on these parameters of the RAF of affected IC_{Rec} neurons according to their type of RAF (Table 2, $P>0.05$, one-way ANOVA).

4. Discussion

In the present study, we examined the effect of inter-collicular suppression on signal processing in amplitude domain using focal electrical stimulation in one IC and electrophysiological recording in the other IC. We used a focal electrical stimulus of 25 μA that has been proved effective and appropriate for studying inter-collicular modulation and corticofugal modulation of collicular signal processing (Jen *et al.* 1998, 2003, Mei *et al.* 2012a, b, Cheng *et al.* 2013). As such, the acoustically evoked responses of electrically stimulated neuron recovered quiet well after cessation of electrical stimulation (Fig. 1A). Under such IC_{ES} electrical stimulation, inter-collicular suppression was activated and the number of impulses of IC_{Rec} neurons were suppressed (Fig. 1B).

The inter-collicular suppression compresses the RAFs of the collicular neurons over a range of sound-stimulus amplitudes (Fig. 2A-2, B-2, C-2) and the degree of compression was greater at low than at high sound stimulus amplitude (Fig. 2A-3, B-3, A-4, B-4, Fig. 3). Conceivably, this observation is probably due to the fact that inter-collicular suppression produces a constant amount of inhibitory input to IC_{Rec} neurons at all sound stimulus amplitude but the effectiveness of suppression progressively decreases when the excitatory input to IC_{Rec} neurons increases with sound amplitude. These indicate that inter-collicular suppression involve in modulating sound-amplitude processing in IC neurons by suppressing the neuron's number of impulses at low-sound-stimulus amplitudes. The similar observations have been reported in previous studies that show the inter-collicular interaction can modulate facilitory and inhibitory effects on collicular neurons and the greatest effects occurs at near-threshold amplitude levels (Malmierca *et al.* 2005, Mei *et al.* 2012a).

Consistent with previous studies, here we observed that IC neurons had three types of RAFs: monotonic, saturated, and non-monotonic (Fig. 2A-2, B-2, C-2) (Phillips and Kelly 1989, Zhou and Jen 2002, Wu and Jen 2009). Inter-collicular suppression did not induce changes in the type of most RAFs of the IC_{Rec} neurons (Table 1). According to previous studies, we know that RAFs (i.e. amplitude tuning) are created primarily by imbalanced synaptic inhibition that is disproportionately large at high-sound-stimulus amplitudes (Oswald *et al*. 2006, Wu *et al*. 2006, Tan *et al.* 2007, 2009, Zhou *et al.* 2012). The inter-collicular suppression here results in less suppression at high sound-stimulus amplitudes, which would not usually change the RAF type of these IC neurons (Plontke *et al.* 1999, Wu and Jen 2007, 2009). However, we did observe a few instances in which IC_{ES} ES did result in a change in RAF type (Table 1). This could have resulted from inhibitory local circuits that become more active with greater acoustic stimulation.

What is the biological significance of inter-collicular suppression in sound-signal processing in each type of IC neuron? The increase in MT, decrease in the DRs, but stable in the BA cause the slope of RAFs increased and the responsive amplitudes narrowed down to high amplitude level. Such alterations would sharpen the sensitivity of all types of IC neurons to variation in high sound amplitude within a narrower range (Fig. 4). Conceivably, the inter-collicular suppression could improve the sensitivity of IC neurons to high amplitude sound as well as to variation in amplitude such as amplitude modulated sound (Rees and Møller 1987, Joris *et al.* 2004, Dean *et al.* 2005). As such, inter-collicular suppression might come into play when the IC neurons receive and encode the high-amplitude acoustic information. However, the alterations on RAFs did not differ cross RAF types, suggesting that these effects of inter-collicular suppression on auditory sensitivity do not depend on the RAF types. The inter-collicular suppression appears to function similarly with inhibitory corticofugal control that has been shown to improve sound-amplitude signal processing of subcortical auditory structures such as the IC, medial geniculate body (MGB), and cochlear nucleus (CN) (Jen *et al.* 1998, Suga *et al.* 2000, Zhou and Jen 2000, 2002, He 2003, Ma and Suga 2007, Luo *et al.* 2008). Presumably, in the IC, the inter-collicular suppression might work with corticofugal inhibition together to modulate the auditory sensitivity of neurons at the same time. In addition, inter-collicular suppression might also help maintain the unilateral dominance of one IC by suppressing the acoustic-evoked responses of neurons in the opposite IC, thus shaping sensitivity to interaural intensity differences, which are needed for sound localization at the azimuth and for binaurally stereoscopic hearing (Irvine *et al.* 1996, Konishi 2000, Grothe 2003, Malmierca *et al.* 2005, Grothe *et al.* 2010). Future studies will be needed to test these predictions.

In this study, the effects of inter-collicular suppression on sound amplitude processing were examined using focal electrical stimulation in one IC and electrophysiological recording in the other IC. The CoIC fibers as the direct pathway from one IC to the other would be activated directly and primarily when electrically stimulating the unilateral IC, which can efficiently mediate the inter-collicular suppression observed in this study (Aitkin and Phillips 1984, Oliver *et al*. 1991, Malmierca *et al*. 2009, Cheng *et al*. 2013). However, there is another possible pathway that can mediate the inter-collicular interactions that is activation of indirect neural circuit involving other auditory nuclei (e.g. corticofugal feedback loop). It is necessary in the future study to test the possible neural pathway by inactivation of ipsilateral auditory cortex with Lidocaine, or ablation of the CoIC during electrical stimulation of IC.

In conclusion, inter-collicular suppression significantly increased the slope, decreased the dynamic range and narrowed down the responsive amplitude of all RAFs to high amplitude level but did not change the type of RAFs. As a result, all types of RAFs were compressed at a greater degree at low than at high sound amplitude during inter-collicular suppression. These data indicate that inter-collicular suppression can improve sound processing of IC neurons in the high amplitude domain regardless of their RAF type.

Conflict of interest

There are no actual or potential conflicts of interest.

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Figure legends

Fig. 1. The response of two representative IC_{ES} and IC_{Rec} neurons under different stimulation condition. (A) The response of a representative IC_{ES} neuron obtained before (a) and recovery (b) from focal electrical stimulation (ES). **(B)** The response of a representative IC_{Rec} neuron obtained before (a) and during (b) focal ES. The response of all these two neurons were obtained with a best frequency (BF) sound delivered at 10 dB above the minimal threshold (MT). N: number of spikes. Lat: latency. Horizontal bar: acoustic stimulus. Arrow: focal electrical stimulation. The BF, MT and recording depth of this neuron were 17.1 kHz, 58 dB SPL, 1670 μm (A); 15.6 kHz, 68 dB SPL, 1510 μm (B); respectively.

Fig. 2. Suppressive modulation of rate–amplitude functions of three types of recorded IC (IC_{Rec}) neurons (A, B, C) during focal IC_{ES} ES. (A-1, B-1, C-1) Post-stimulus-time histograms of responses from three representative IC_{Rec} neurons to best frequency (BF) sounds (horizontal bar under abscissa) delivered at 10 dB above each neuron's minimal threshold (MT) before (A-1a, B-1a, C-1a; arrows on A-2a, B-2a, C-2a) and during (up-arrow under abscissa; A-1b, B-1b, C-1b; arrows on A-2b, B-2b, C-2b) focal IC_{ES} ES. *N*, number of impulses. **(A-2, B-2, C-2)** Rate–amplitude functions (RAFs) (monotonic, saturated, and non-monotonic) of the three representative IC_{Rec} neurons before (unfilled circle) and during (filled circle) focal IC_{ES} ES. *n*, number of neurons. **(A-3, B-3, C-3)** Percent suppression of the number of impulses caused by focal IC_{ES} ES for the three representative IC_{Rec} neurons at different stimulus amplitudes. **(A-4, B-4, C-4)** Mean percent suppression of the number of

impulses caused by focal IC_{ES} ES for the three types of IC_{Rec} RAFs at different stimulus amplitudes. Numbers above each standard deviation bar indicate number of neurons. The *P*-value was obtained after a one-way ANOVA. The BFs, MTs, and recording depths of these three neurons were 16.7 kHz, 44 dB SPL, 1270 μm (A); 13.6 kHz, 29 dB SPL, 1691 μm (B); 13.5 kHz, 54 dB SPL, 1011 μm (C).

Fig. 3. Mean percent suppression of spikes in non-monotonic IC_{Rec} neurons during focal IC_{ES} ES. Bars show the mean percent suppression in spikes caused by focal IC_{ES} ES for two ranges of stimulus amplitude: ≤20 dB above each neuron's MT and ≥30 dB above each neuron's MT. *n*, the number of neurons; ***, $P<0.001$ (paired *t*-test).

Fig. 4. Distribution of different parameters for the three types of IC_{Rec} neurons before and after focal IC_{ES} ES. A-1–A-5, B-1–B-5, C-1–C-5 show the distribution of MT, BA, DR, mDR, and slope of RAFs for the three types of IC_{Rec} neurons (A, monotonic, B, saturated; C, non-monotonic) before (unfilled circles) and during (filled circles) focal IC_{ES} ES. The bars in each panel are the mean value of each parameter. *n*, the number of neurons. *, $P<0.05$, **, $P<0.01$, ***, $P<0.001$ (paired *t*-test).

Table 1 Types of RAFs of IC_{Rec} neurons before and during focal IC_{ES} ES

	before ES	during ES		
		Monotonic	Saturated	Non-monotonic
	n= (%)			
Monotonic	19 (44.2)	15 (34.9)	3 (7.0)	1 (2.3)
Saturated	12 (27.9)	2 (4.6)	10 (23.3)	0 (0)
Non-monotonic	12 (27.9)	0 (0)	1 (2.3)	11 (25.6)
total	43 (100)	17 (39.5)	14 (32.6)	12 (27.9)

n, number of IC_{Rec} neurons

Table 2 Comparison of percent change in MT, BA, DR, mDR and Slope across three types of RAFs of IC_{Rec} neurons due to IC_{ES} stimulation

		Monotonic	Saturated	Non-monotonic	*P*
	n	19	12	12	
MT (dB SPL)	Range	1.3–38.9	1.3–58.8	0–48	
	Mean±SD	11.4±8.9	15.2±16.7	13.6±13.1	>0.05
BA (dB SPL)	Range	0–10.5	0–10.5	0–35.7	
	Mean±SD	0.9±2.7	1.8±3.4	4.0±10.6	>0.05
DR (dB)	Range	10.1–59.6	4.5–68.9	1.9–73.5	
	Mean±SD	28.3±15.6	25.6±21.9	37.0±22.8	>0.05
mDR (dB)	Range	0.5–14.0	1.7–17.4	2.0–48.3	
	Mean±SD	5.7±4.1	7.9±6.0	12.7±12.7	>0.05
Slope (% / dB)	Range	5.2–81.4	0.2–253.3	5.8–153.9	
	Mean±SD	33.3±22.5	50.6±72.0	44.1±43.2	>0.05

n, number of IC_{Rec} neurons. *P*, significant level (one-way ANOVA).

Figure 1

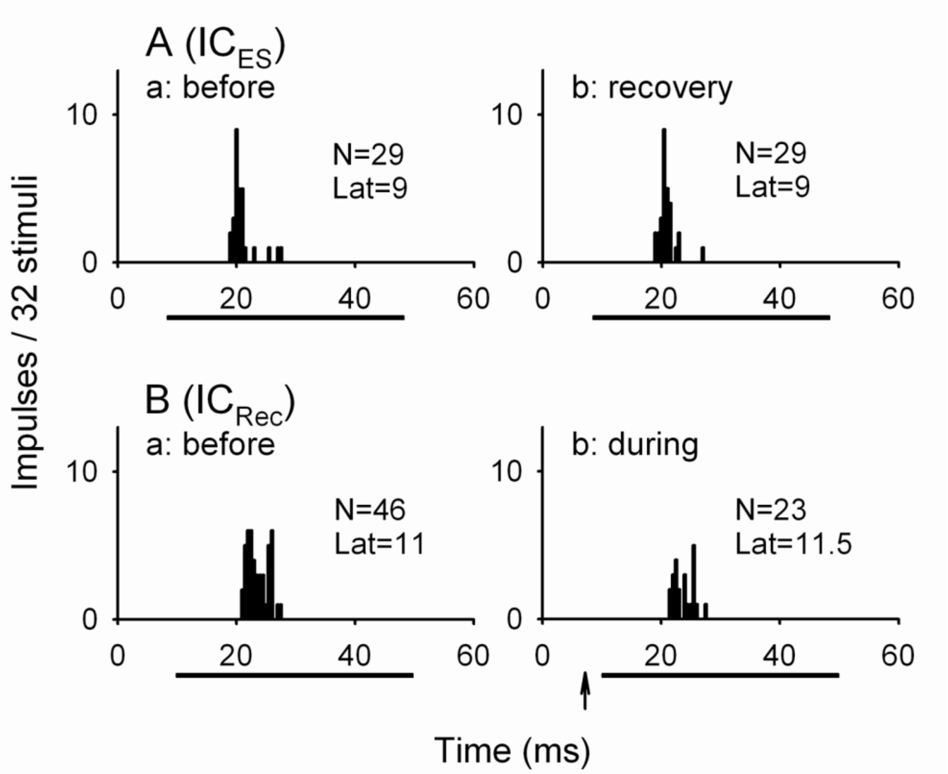
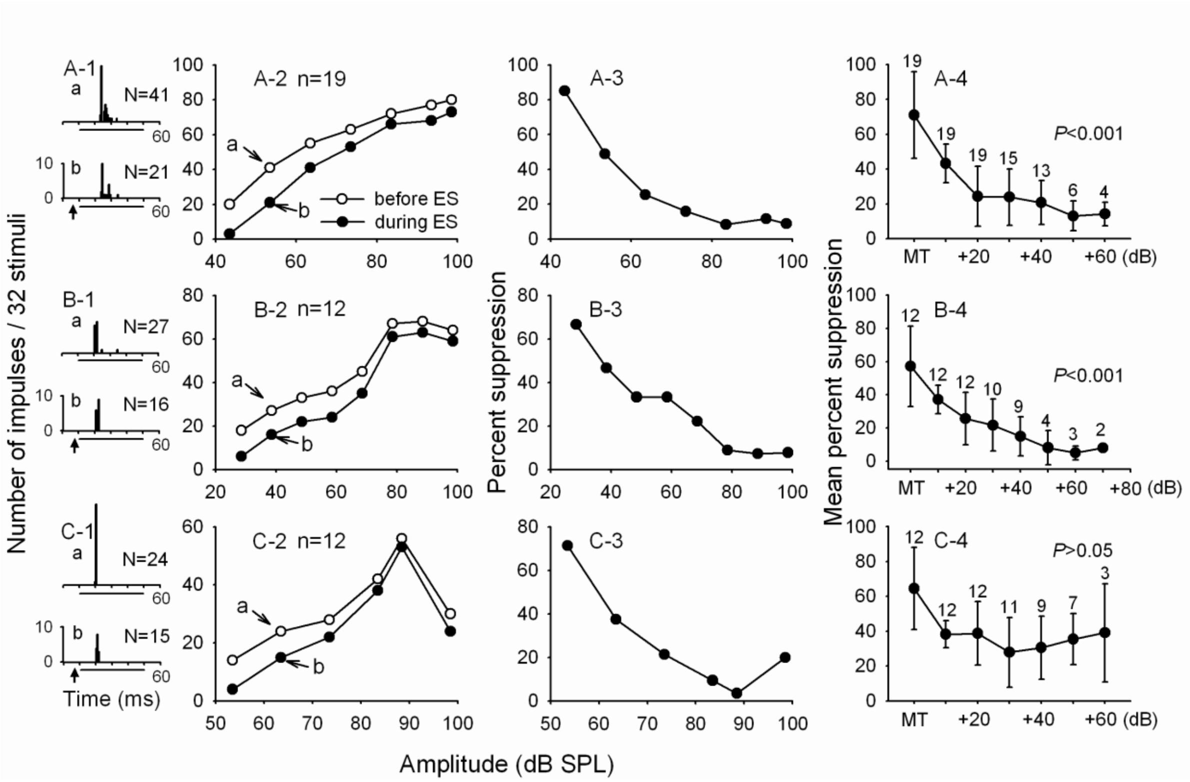

A (IC$_{ES}$)
a: before
b: recovery
N=29
Lat=9
N=29
Lat=9
B (IC$_{Rec}$)
a: before
b: during
N=46
Lat=11
N=23
Lat=11.5
Impulses / 32 stimuli
Time (ms)
0
10
0
20
40
60

Figure 2



A-1
a
N=41
60
10
b
N=21
0
60
A-2 n=19
a
b
before ES
during ES
A-3
A-4
19
19
19
15
13
6
4
P<0.001
MT
+20
+40
+60 (dB)
B-1
a
N=27
60
10
b
N=16
0
60
B-2 n=12
a
b
B-3
B-4
12
12
12
10
9
4
3
2
P<0.001
MT
+20
+40
+60
+80 (dB)
C-1
a
N=24
60
10
b
N=15
0
60
Time (ms)
C-2 n=12
a
b
C-3
C-4
12
12
12
11
9
7
3
P>0.05
MT
+20
+40
+60 (dB)
Number of impulses / 32 stimuli
Percent suppression
Mean percent suppression
Amplitude (dB SPL)

Figure 3

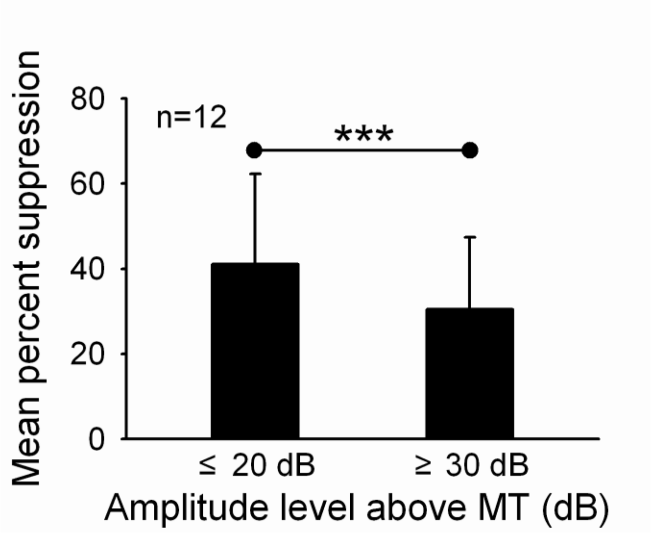
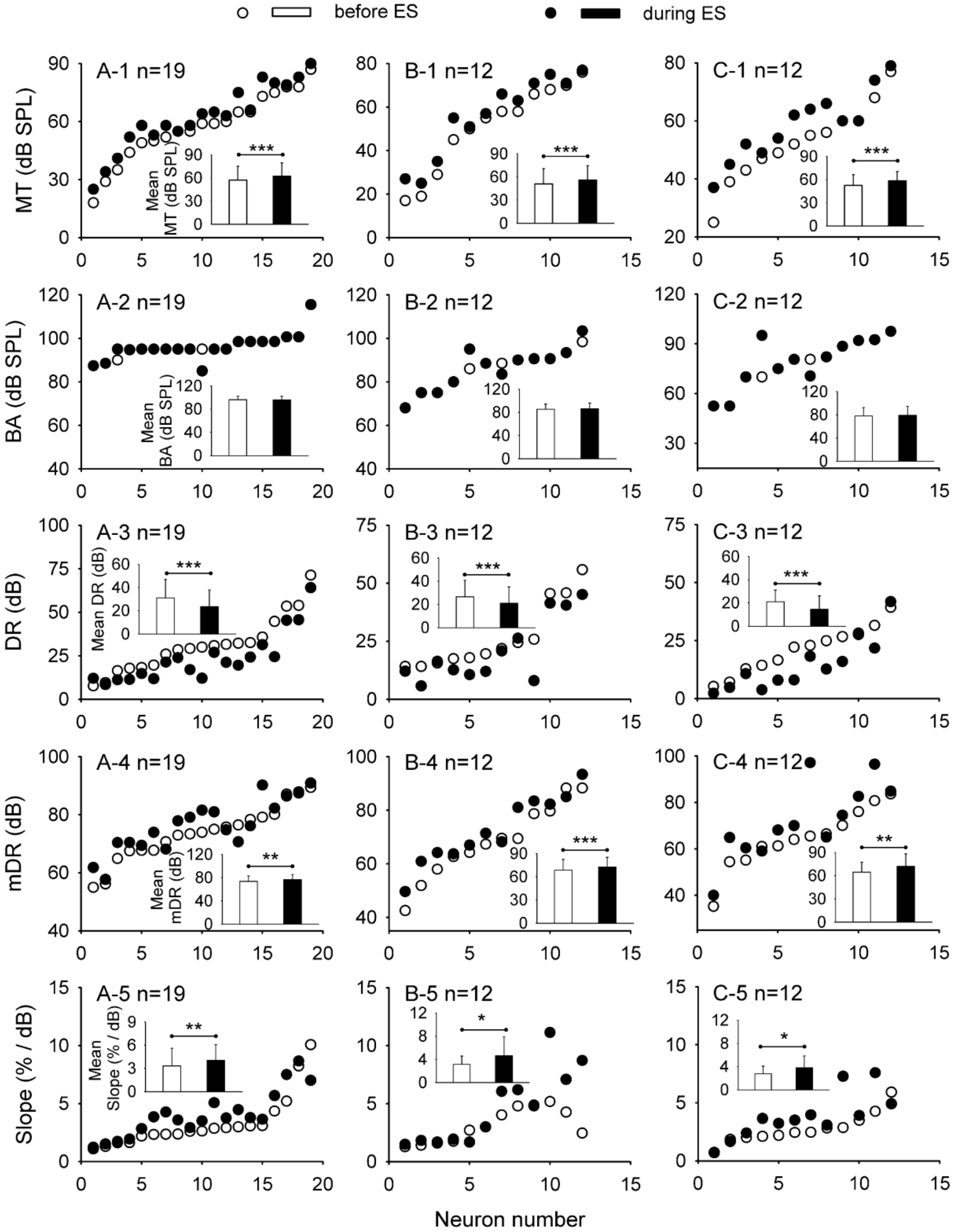

Mean percent suppression
80
60
40
20
0
n=12
***
≤ 20 dB
≥ 30 dB
Amplitude level above MT (dB)

Figure 4


○ ▭ before ES
● ■ during ES
A-1 n=19
B-1 n=12
C-1 n=12
MT (dB SPL)
Mean MT (dB SPL)
***
A-2 n=19
B-2 n=12
C-2 n=12
BA (dB SPL)
Mean BA (dB SPL)
A-3 n=19
B-3 n=12
C-3 n=12
DR (dB)
Mean DR (dB)
***
A-4 n=19
B-4 n=12
C-4 n=12
mDR (dB)
Mean mDR (dB)
**
***
A-5 n=19
B-5 n=12
C-5 n=12
Slope (% / dB)
Mean Slope (% / dB)
*
Neuron number