Plasticity in the developing auditory system

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Outline

1. Critical periods for plasticity

2. Deviance detection and predictive processing

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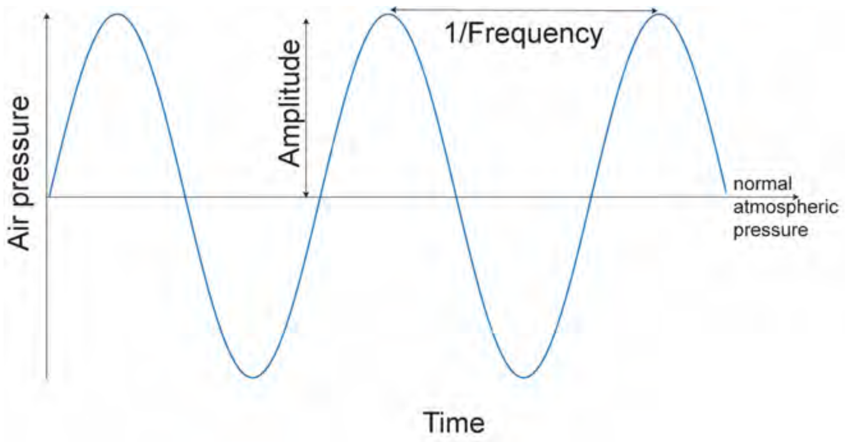
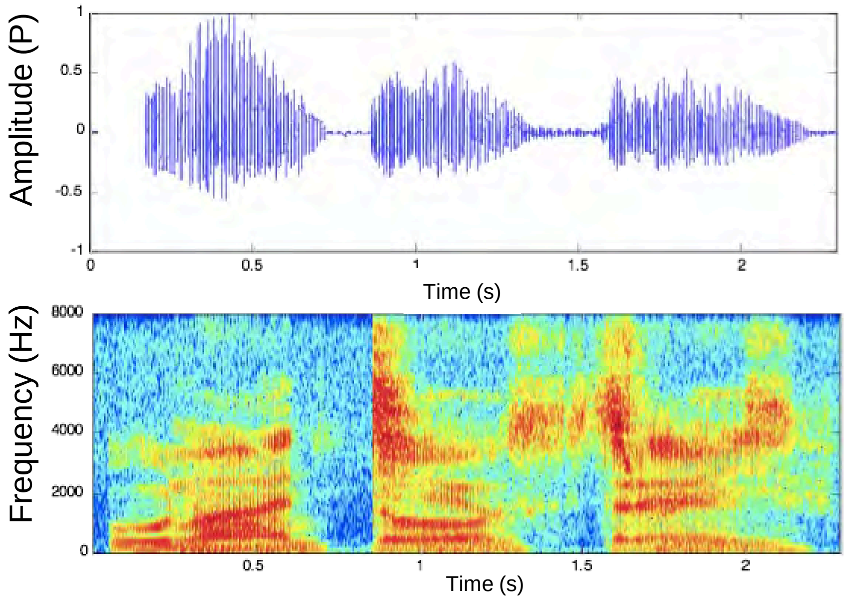
2. Deviance detection and predictive processing

Sound

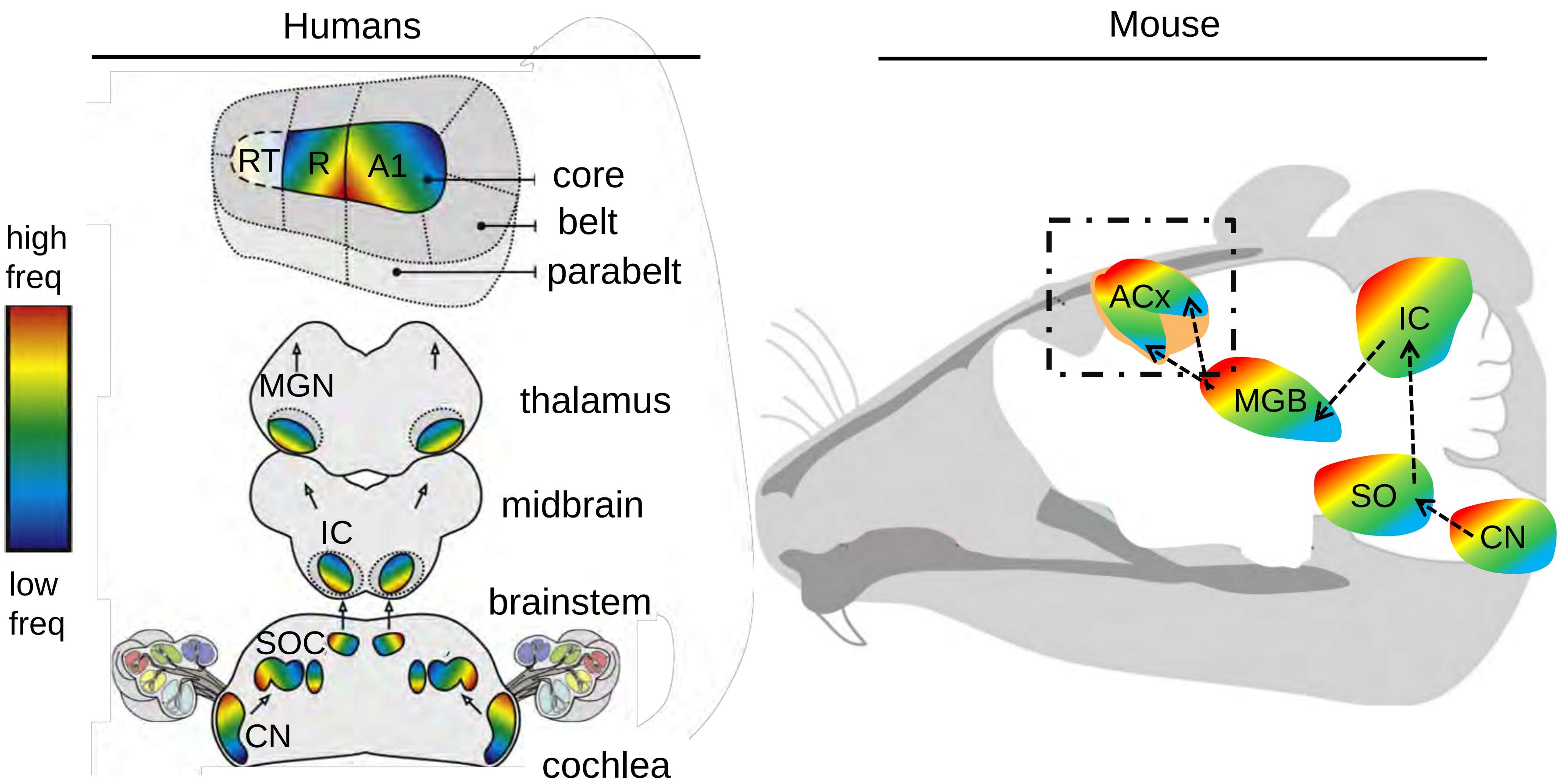
Waveform of a pure frequency tone



Waveform and spectrogram of human voice

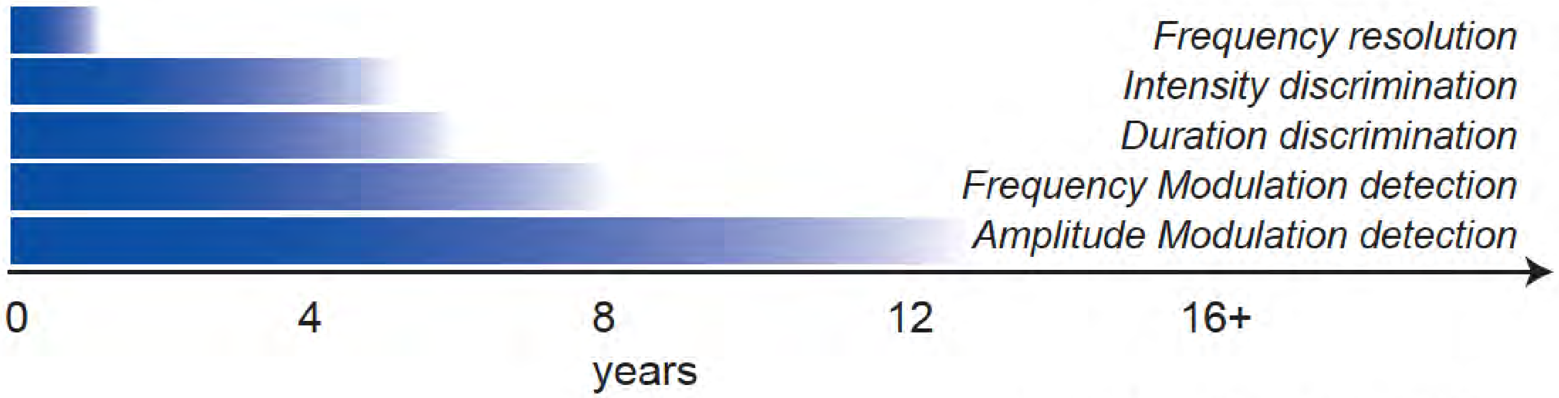


Tonotopy



Humans
Mouse
high freq
low freq
RT
R
A1
core
belt
parabelt
MGN
thalamus
IC
midbrain
brainstem
SOC
CN
cochlea
ACx
MGB
IC
SO
CN

Auditory responses emerge sequentially



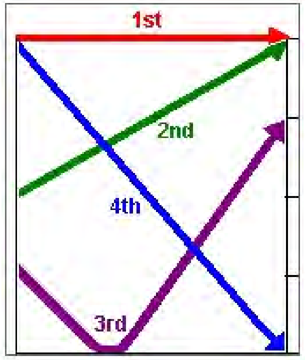
adapated from [Sanes et al, 2011]

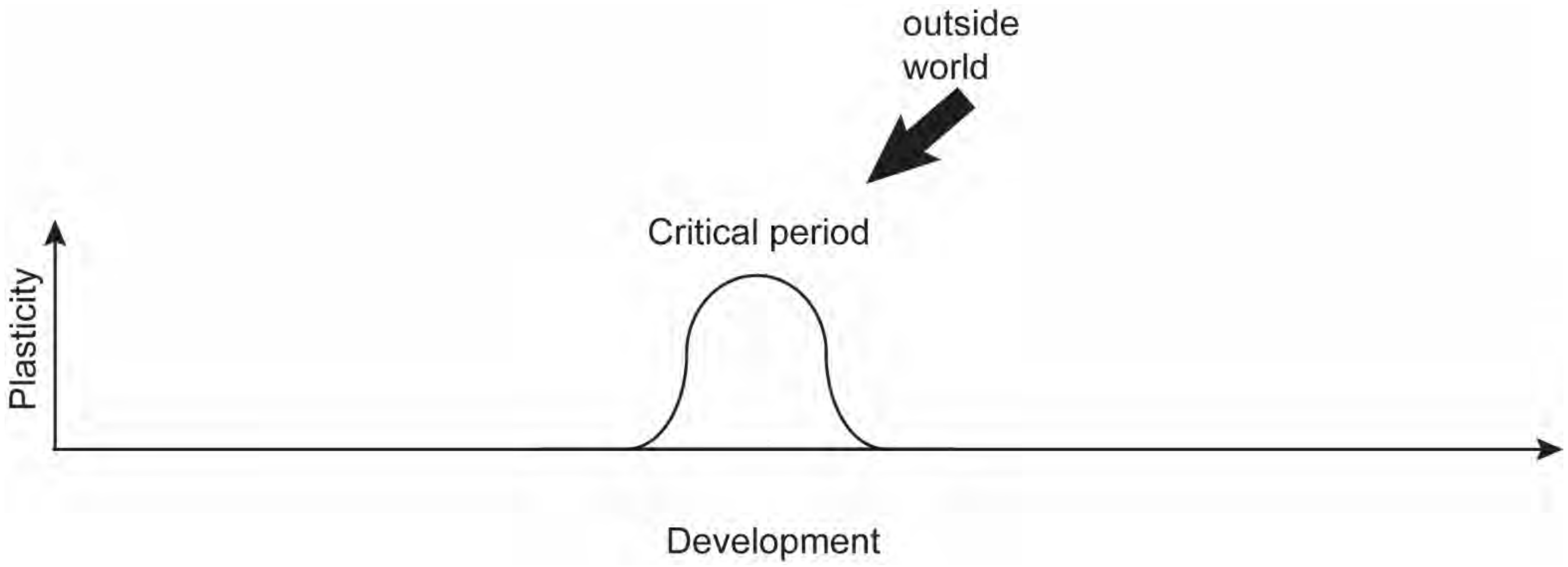
Auditory responses are shaped during development

/la/ and /ra/ distinction

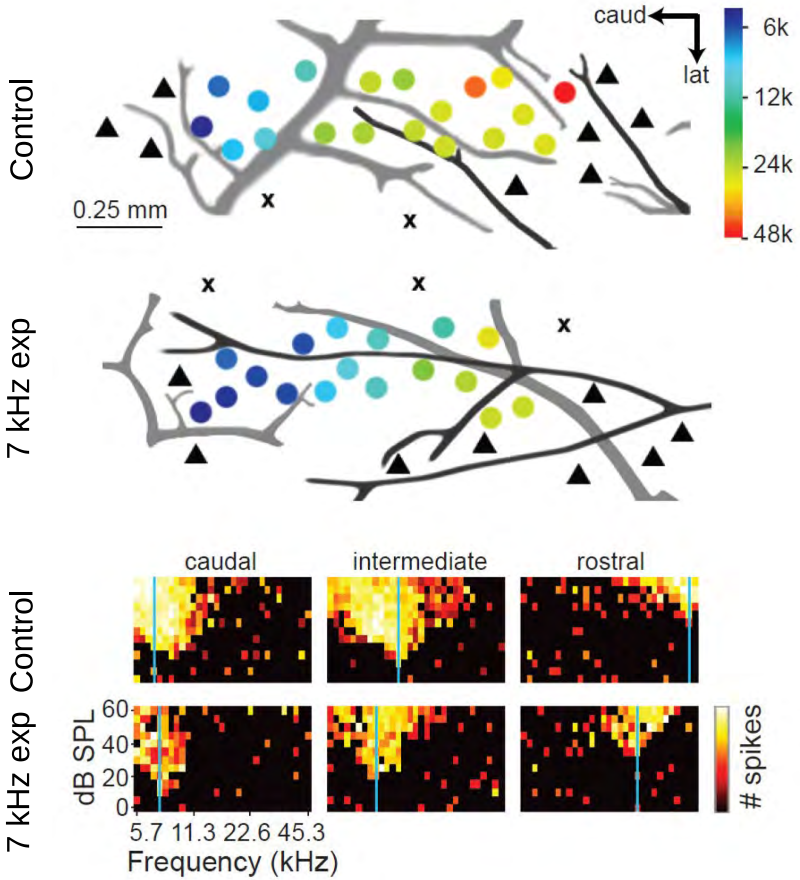
媽 and 馬 distinction

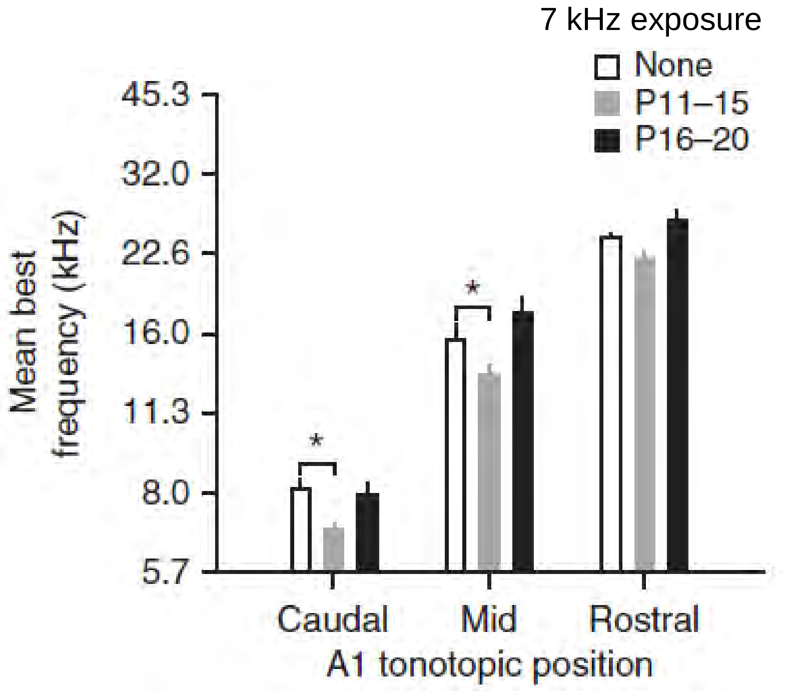
Word with tone	English meaning	Description of tone	Name of tone
mā	Mother	High and level	1st tone
má	To bother	Rising from middle to high	2nd tone
mǎ	Horse	First falling then rising	3rd tone
mà	To scold	Falling from high	4th tone
ma	An interrogative particle	Brief and soft	Neutral





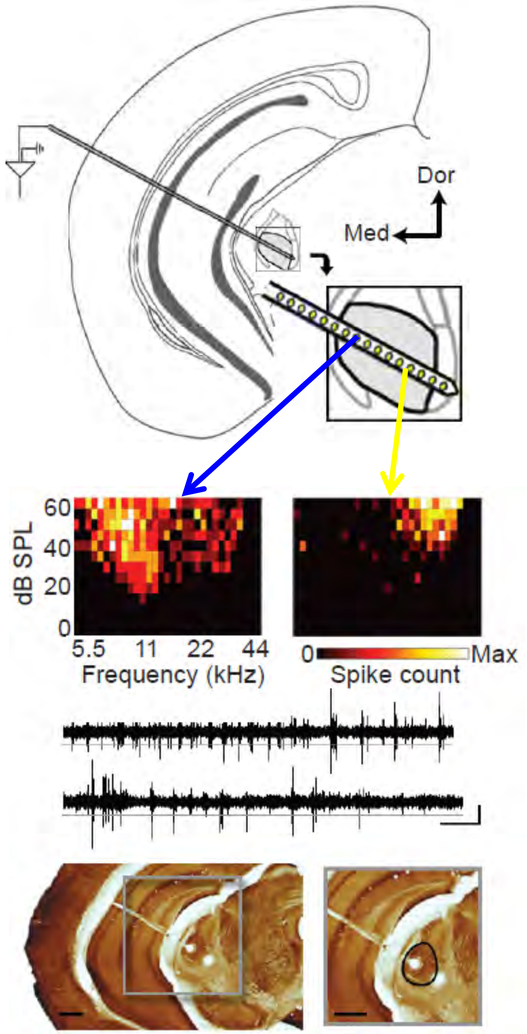
Cortical tonotopic maps reorganize during the critical period for pure tone

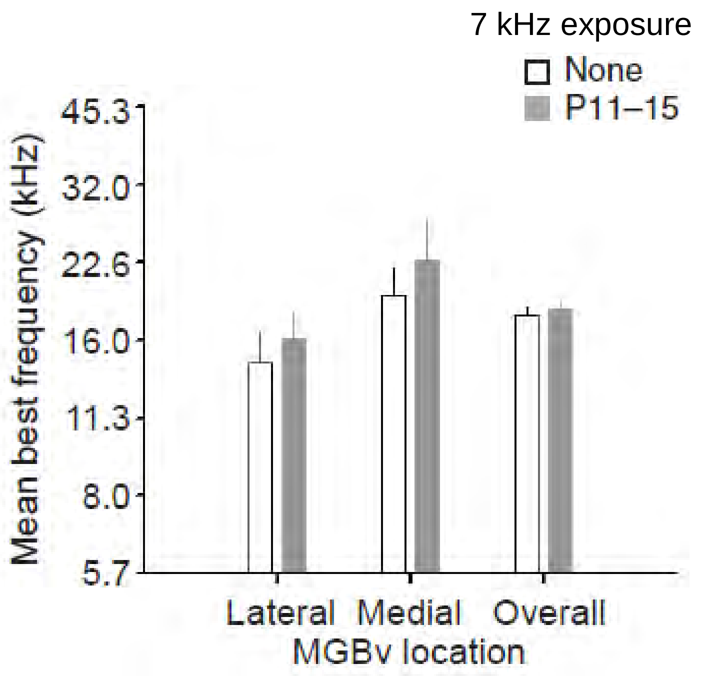




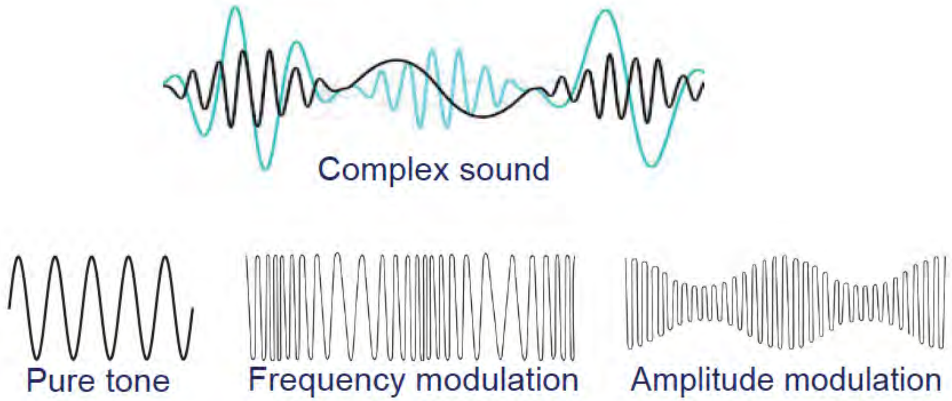
[Barkat et al, 2011]

Thalamic tonotopy remains stable despite reorganization of cortical maps





[Barkat et al, 2011]


Complex sound
Pure tone
Frequency modulation
Amplitude modulation

1. Are there distinct critical periods for plasticity in the auditory system?

2. What are the underlying neuronal circuits?

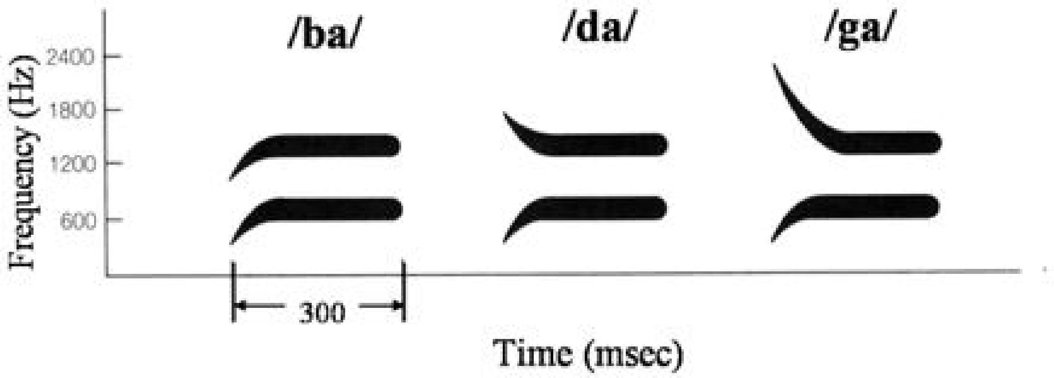
3. How dependent are the different critical periods on each other?

Mari Nakamura

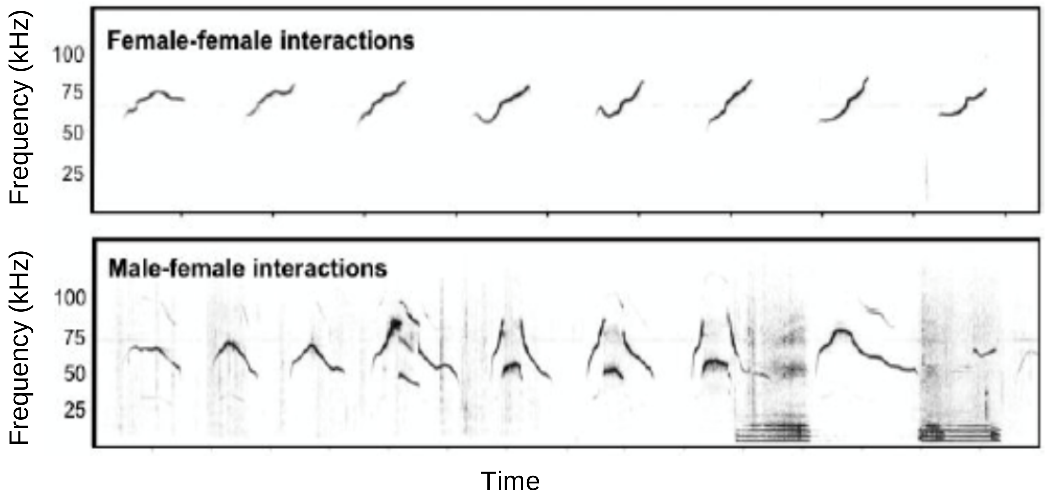
Patricia Valerio

Stitipragyan Bhumika

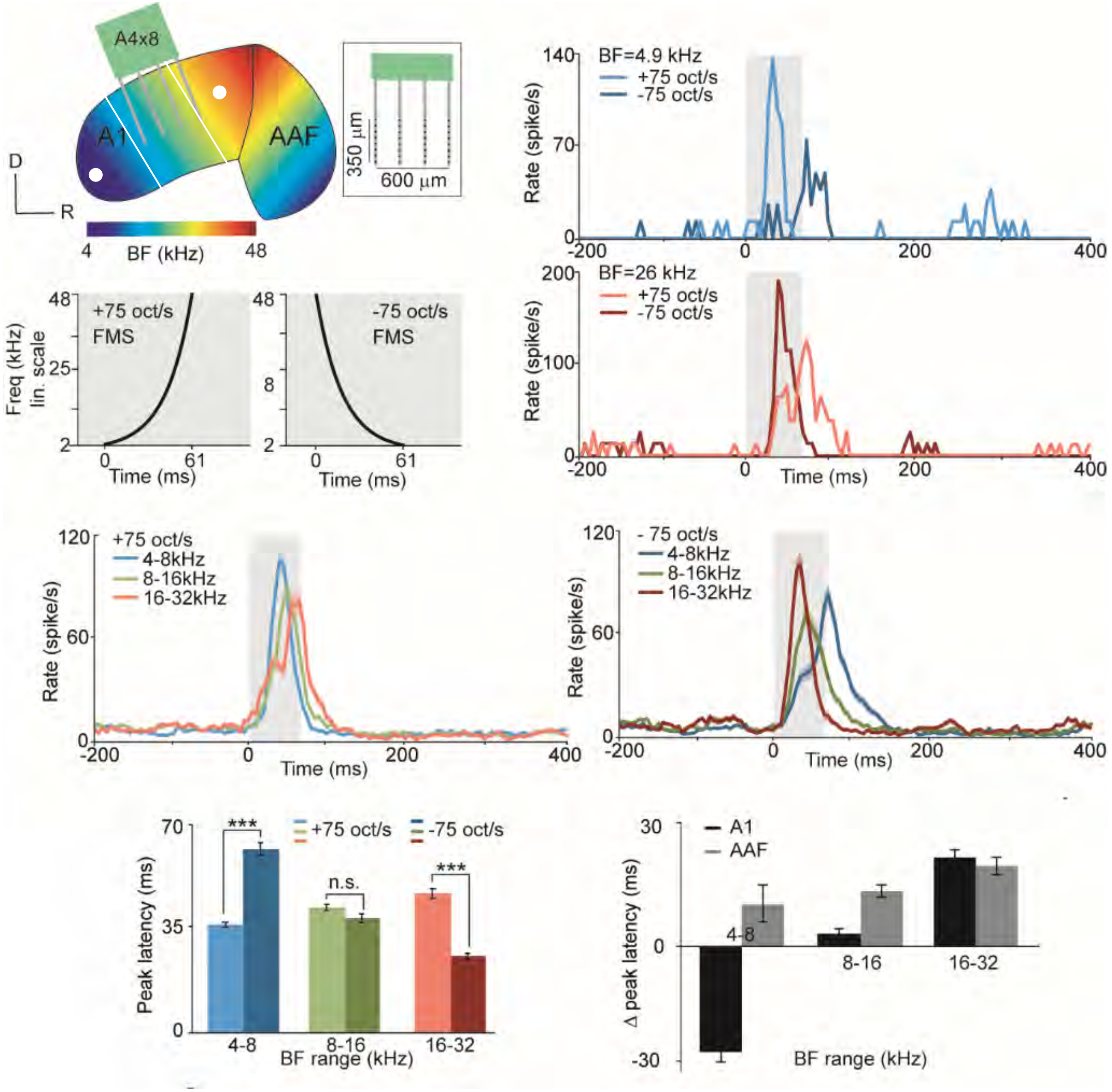
Frequency Modulated Sweeps



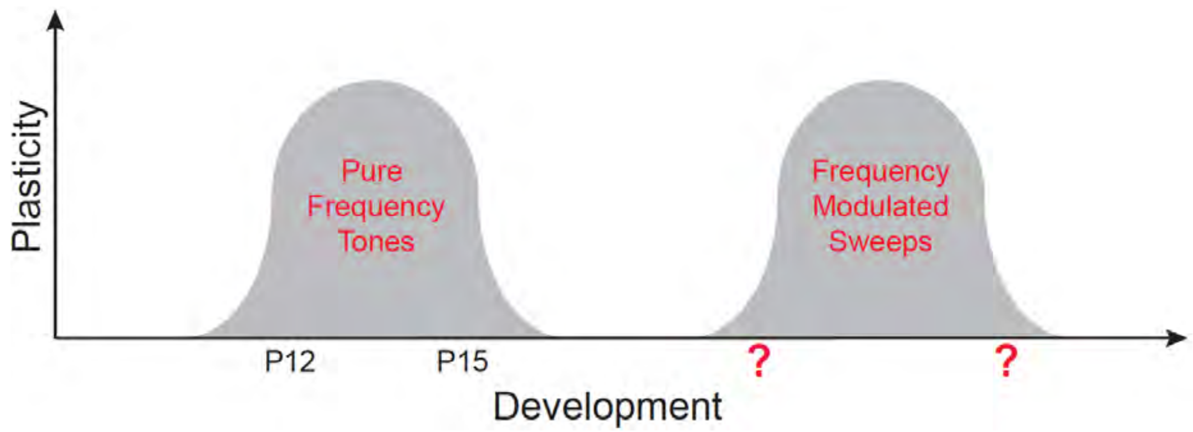
Spectrogram of mouse calls



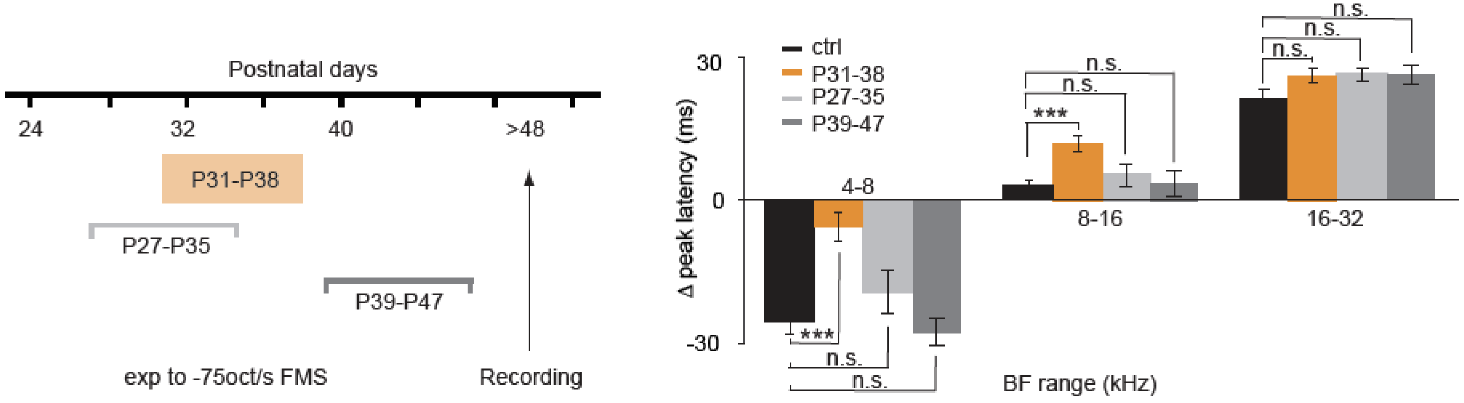
The direction preference to frequency modulated sweeps is spatially organized in A1

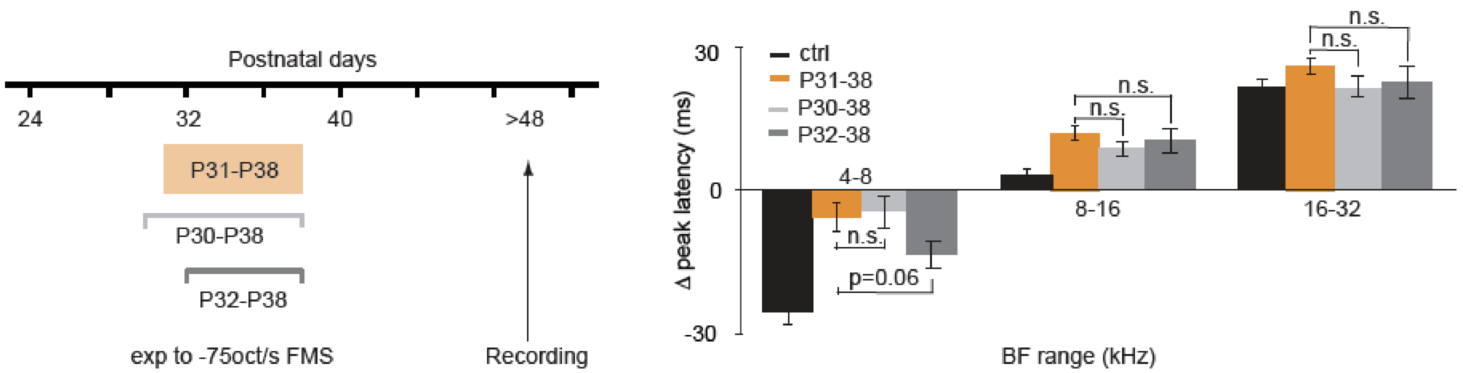


Is there a critical period for FMS?



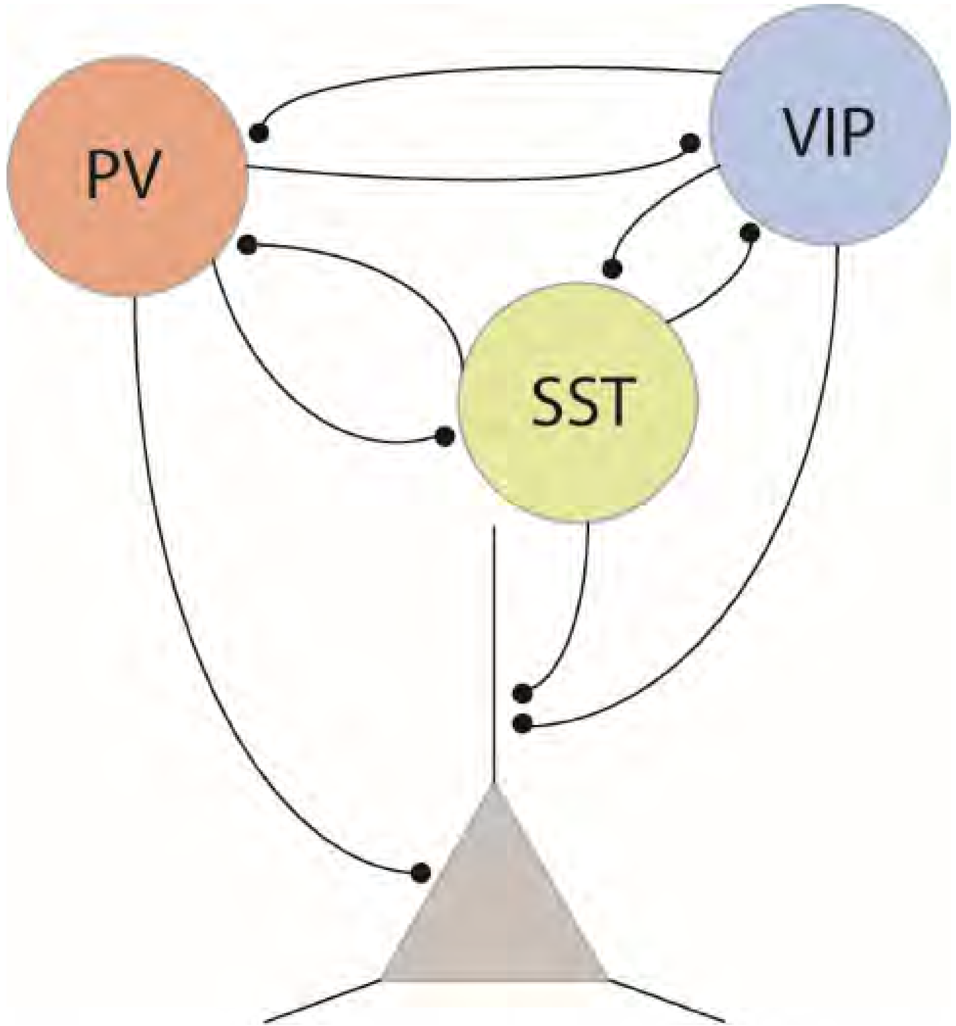
The critical period for FMS direction is P31-P38



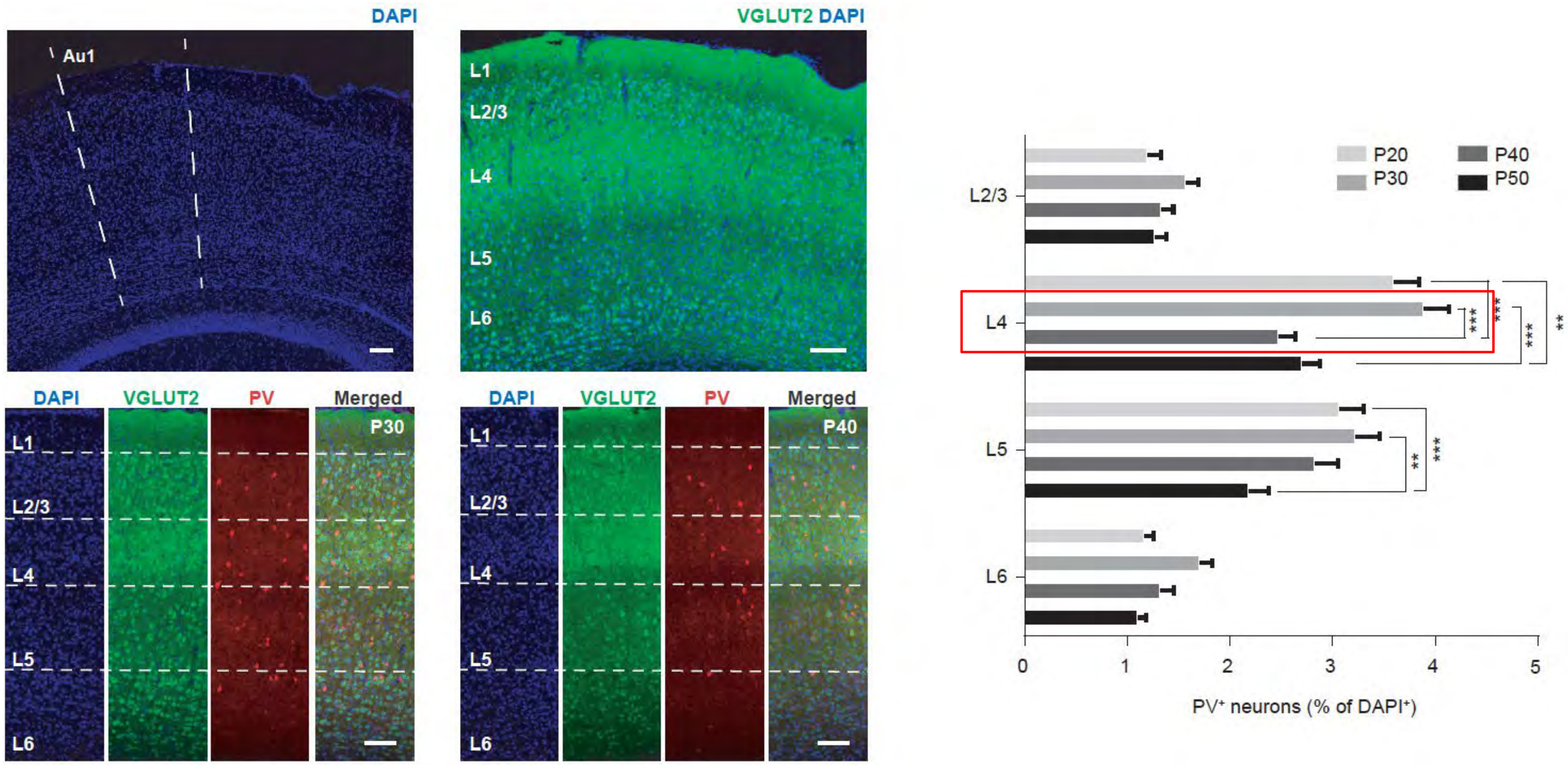


[Bhumika et al, 2019]

What are the underlying neuronal circuits?

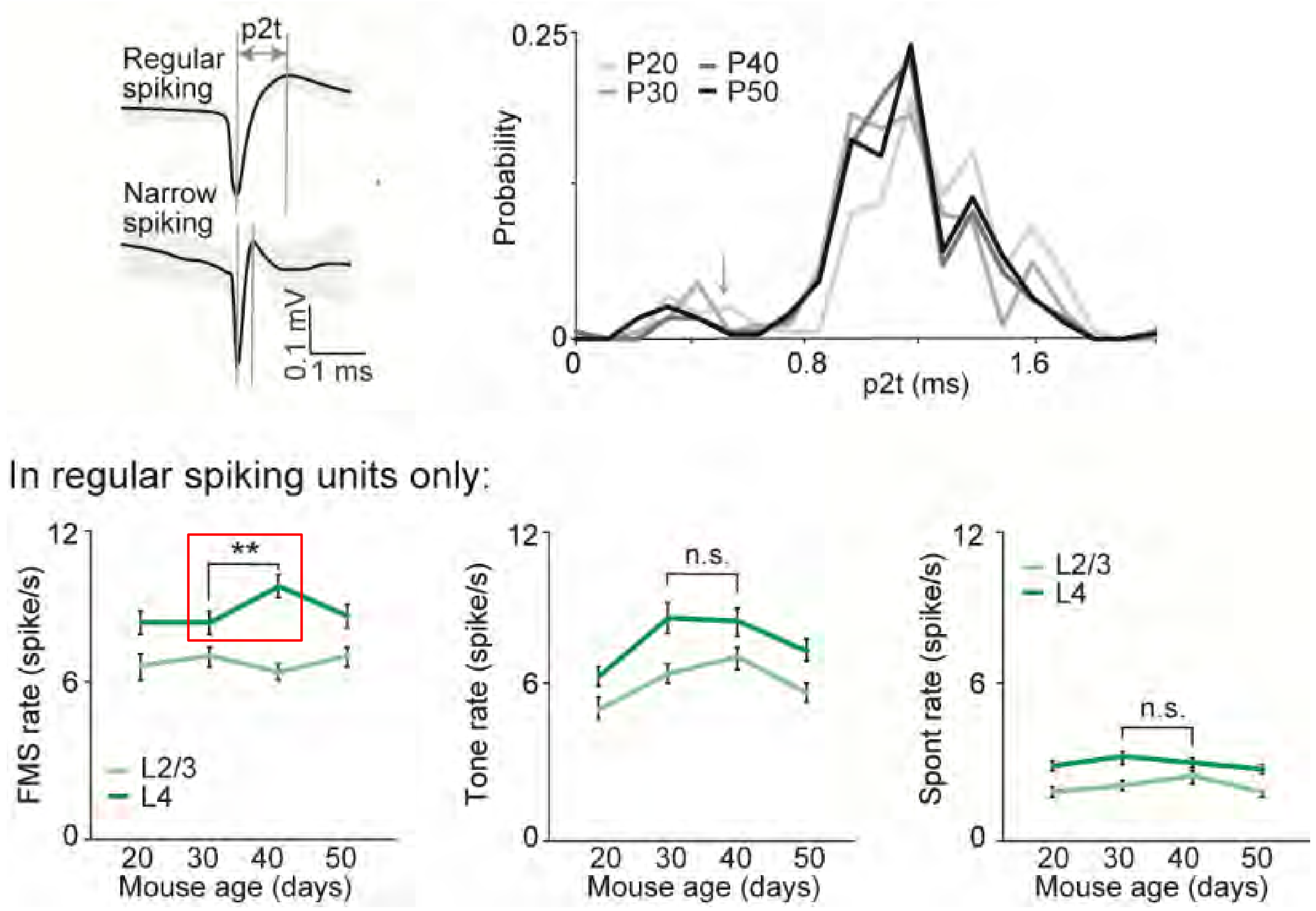


The critical period for FMS is correlated with a decrease in A1 L4 PV^{+} expression

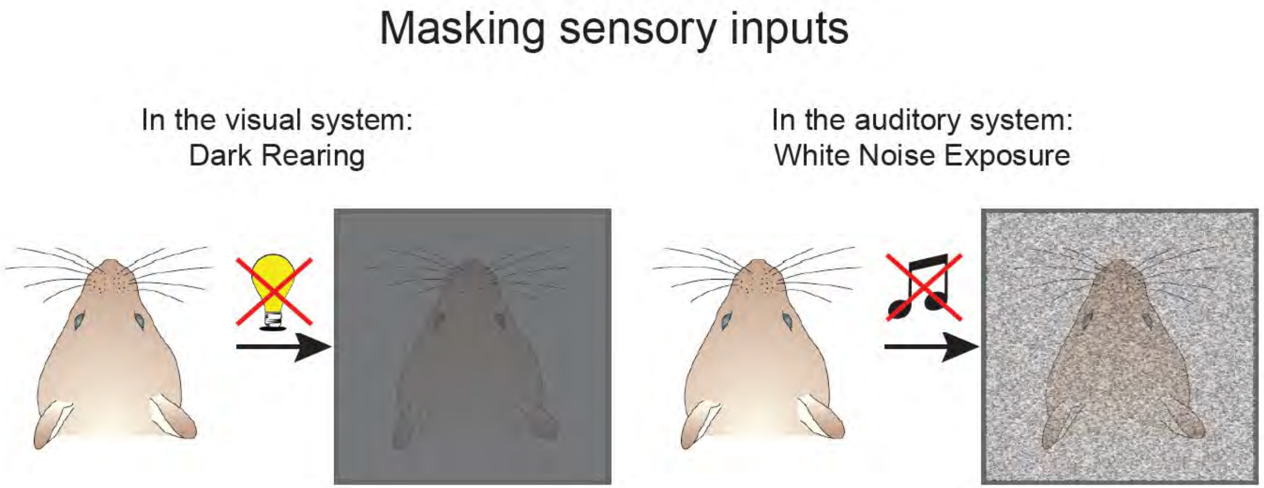


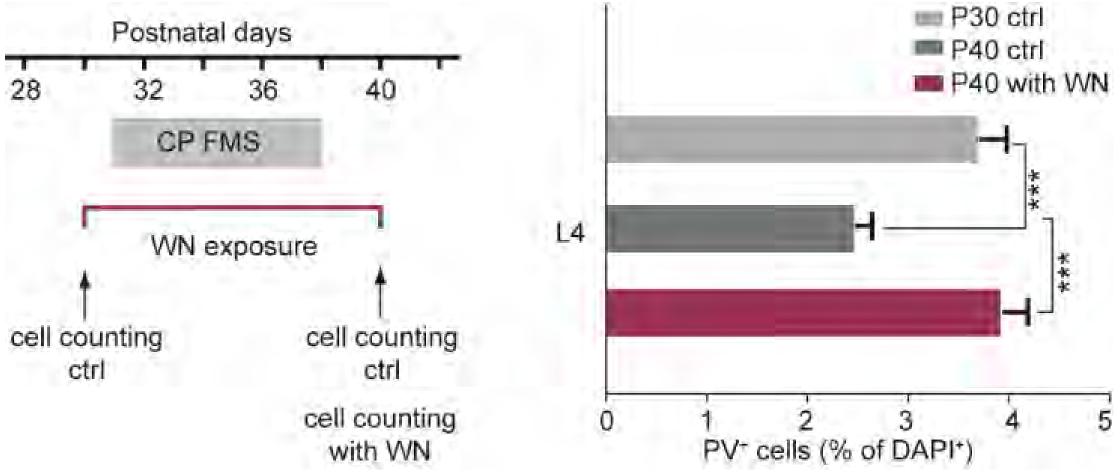
[Bhumika et al, 2019]

L4 excitatory neuron responses to FMS transiently increase during the critical period



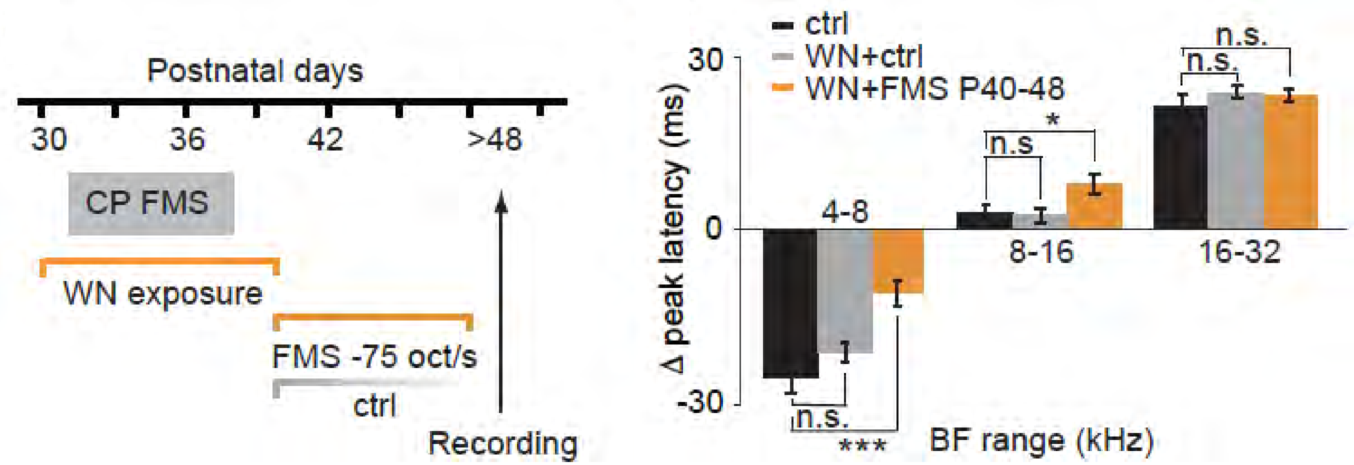
Exposure to continuous white noise delays auditory cortex maturation





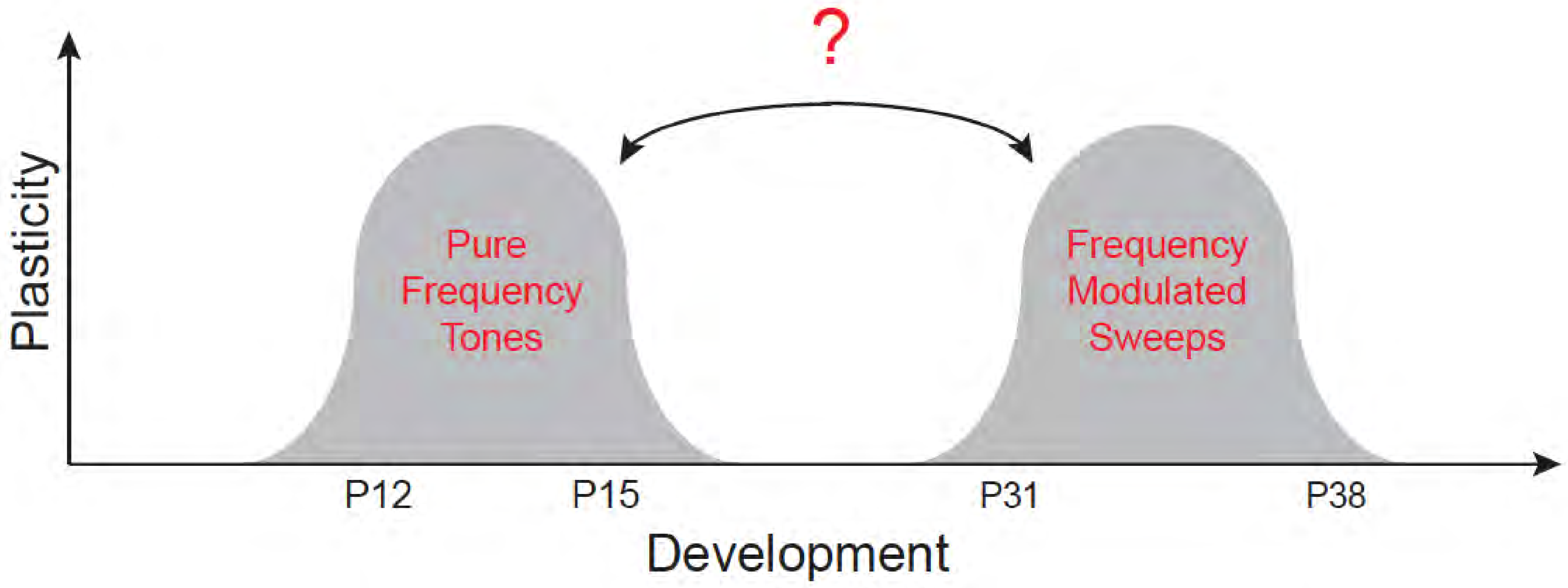
[Bhumika et al, 2019]

Preventing the decrease in L4 PV+ cells delays the critical period for FMS

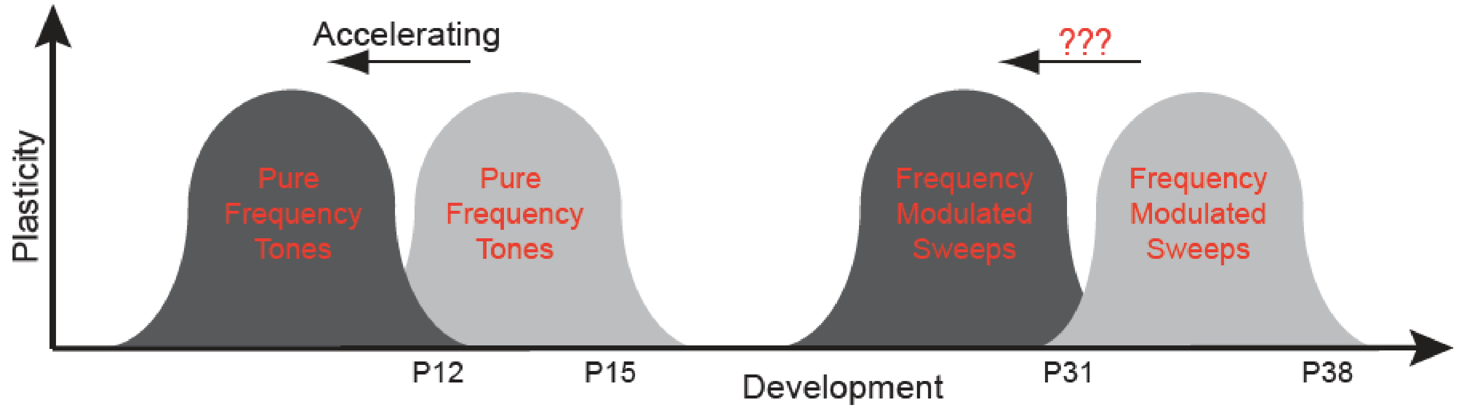


[Bhumika et al, 2019]

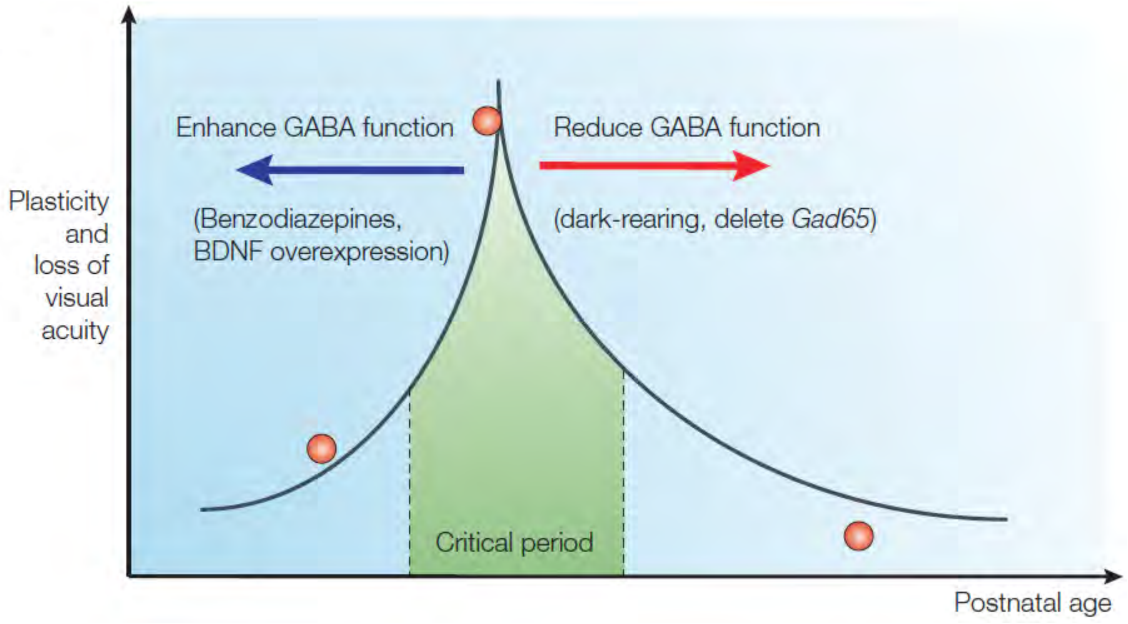
How dependent are the different critical periods on each other?

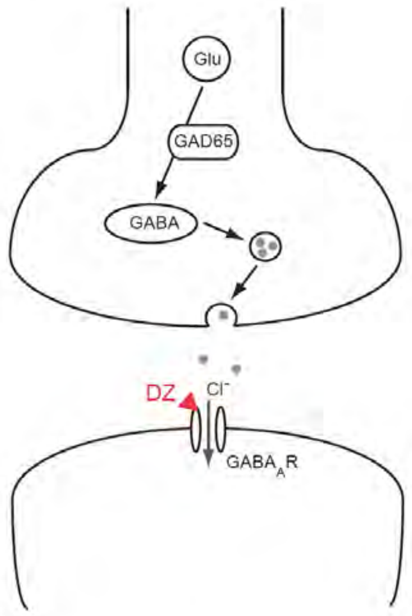


Does accelerating the critical period for pure tone affect the critical period for FMS?



Controlling critical period time window: the role of inhibition

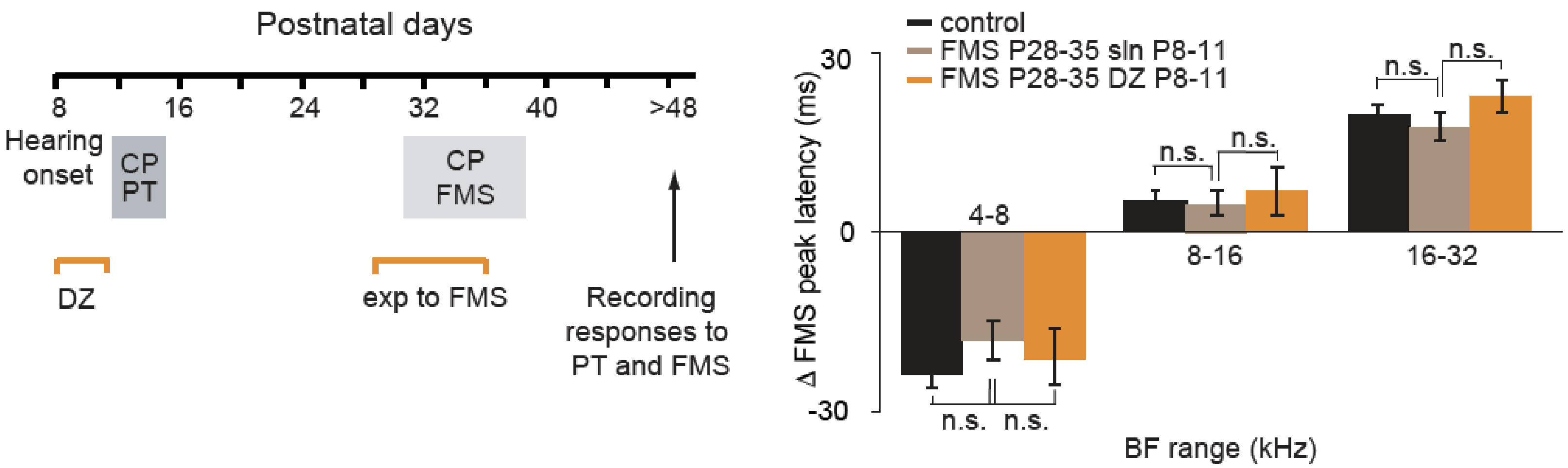




DZ: Diazepam

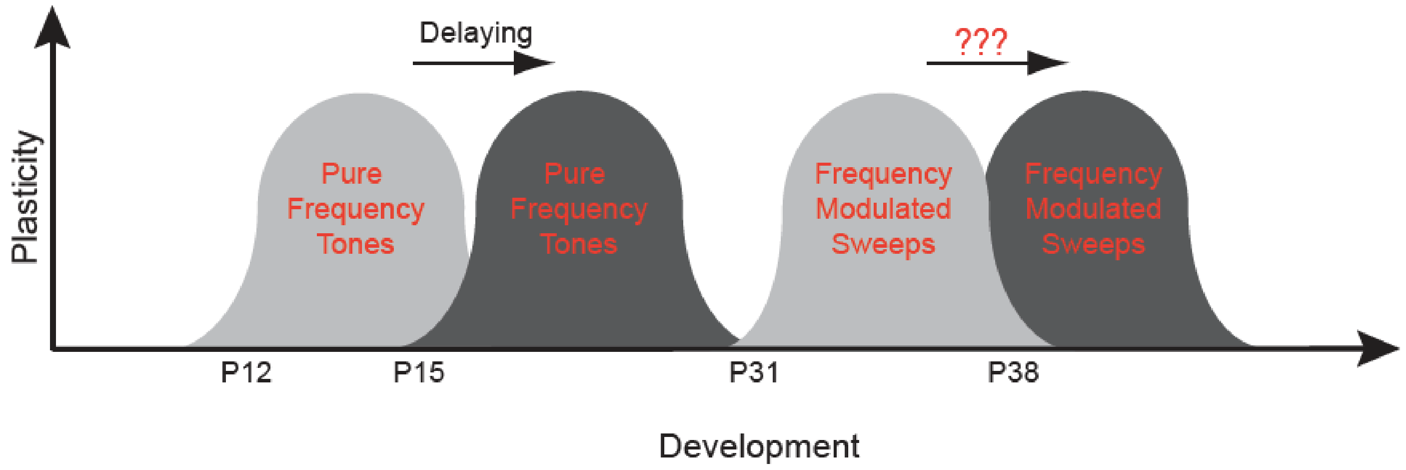
[Hensch, *Nat Rev Neurosci*, 2005]

Accelerating critical period for pure tones does not affect critical period for FMS

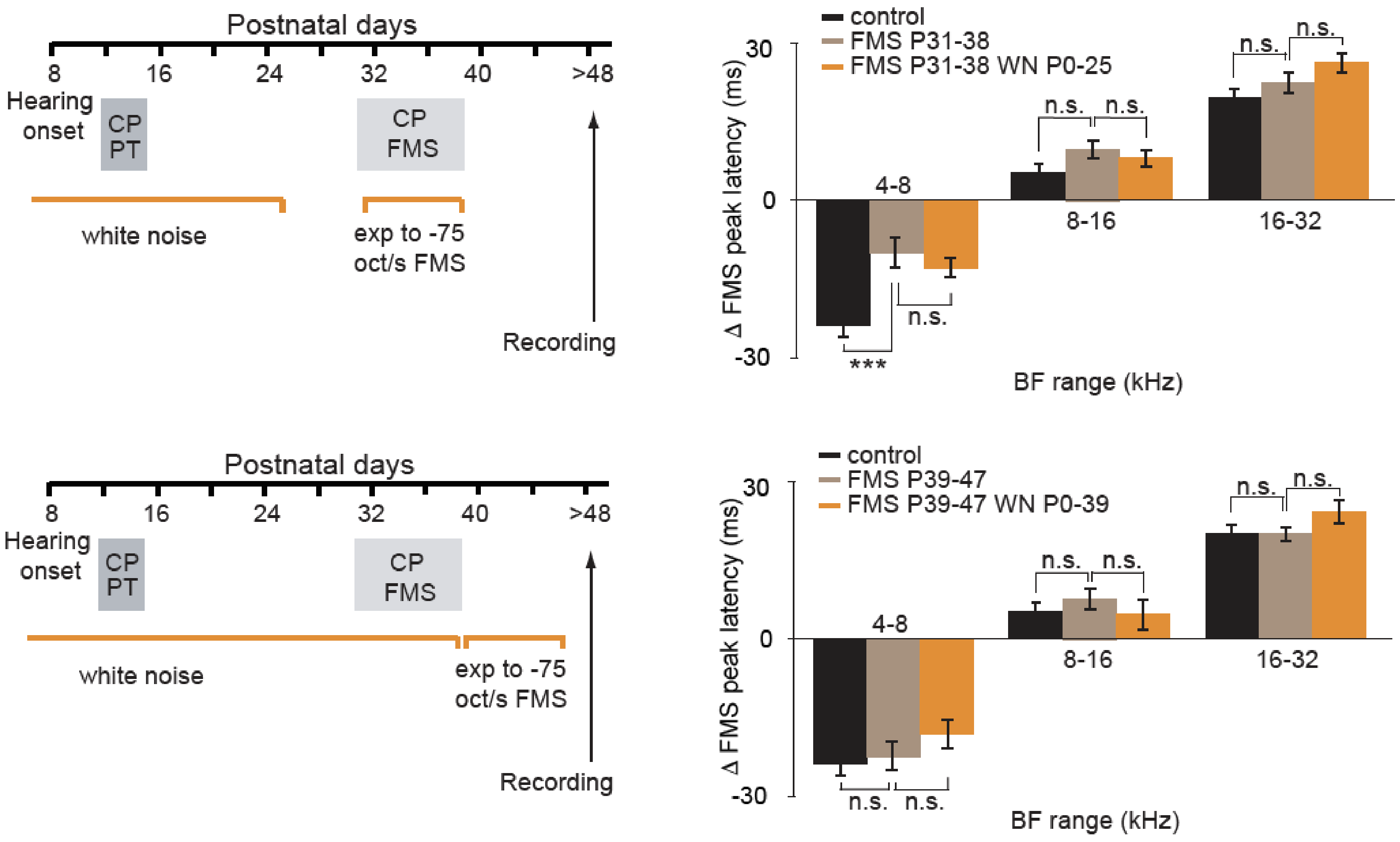


[Nakamura et al, 2020]

Does delaying the critical period for pure tone affect the critical period for FMS?



Delaying critical period for pure tone does not affect critical period for FMS



[Nakamura et al, 2020]

The auditory system has distinct critical periods.

Critical periods are linked to a E/I imbalance of the neuronal circuits encoding the related sound features.

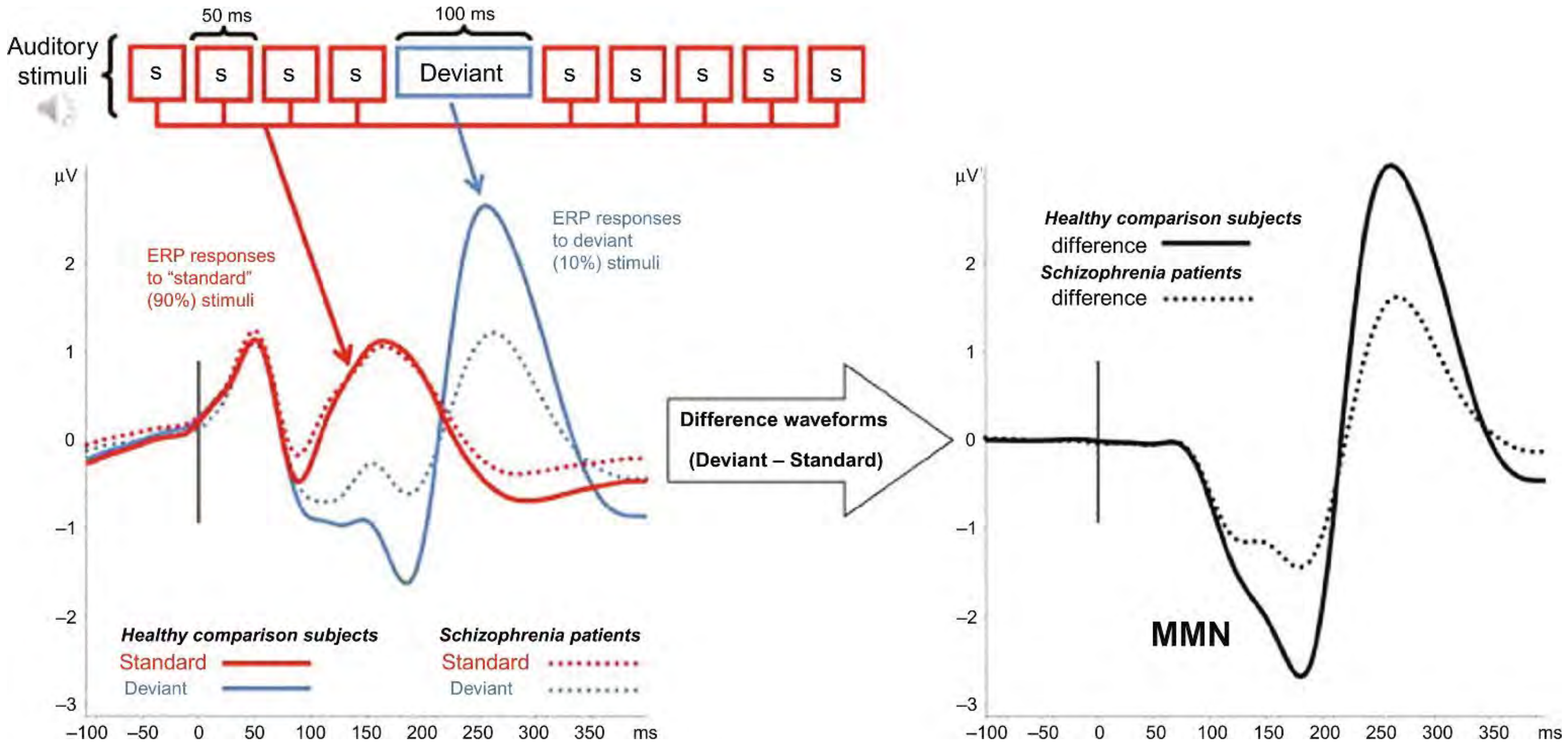
Critical periods are timed by an independent, temporally precise development program.

Outline

1. Critical periods for plasticity
2. Deviance detection and predictive processing

What is deviance detection?

Abnormal deviance detection is associated with developmental disorders

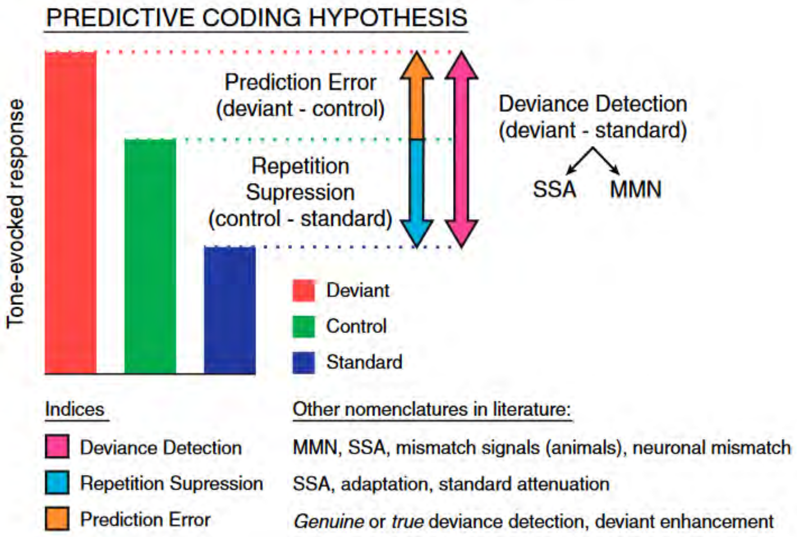


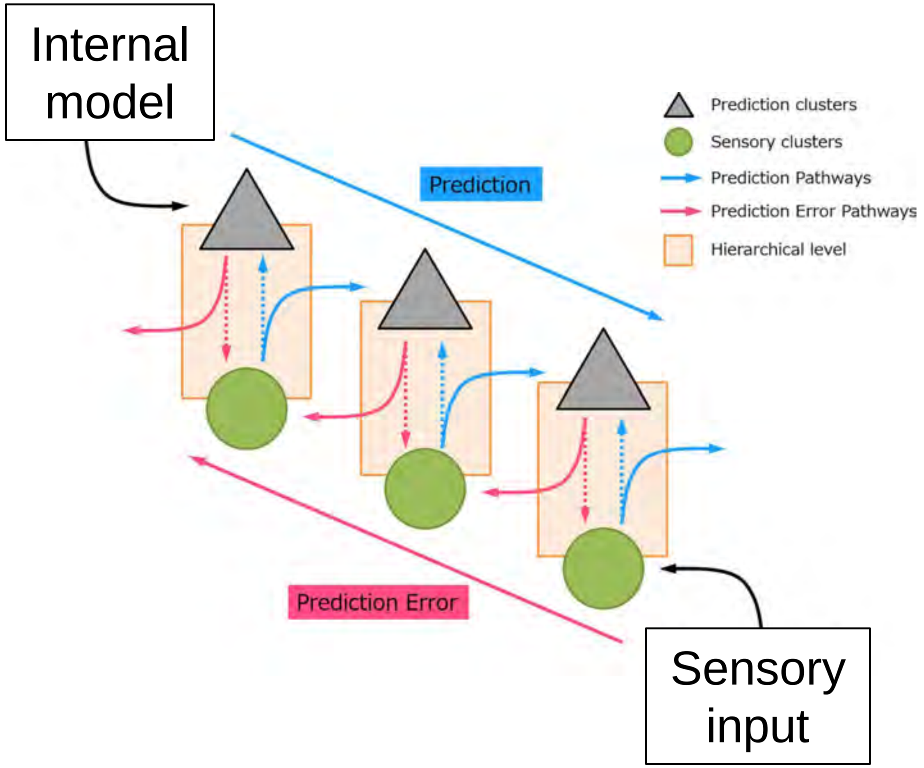
[Light et al., 2015]

Deviance detection combines repetitive suppression and prediction error

Repetition suppression (or stimulus specific adaptation):
- decrease response to the standard sound upon repetition (adaptation)
- The decrease does not generalize to the deviant sound

Prediction error (or 'true' deviance detection):
- Increase in response to the deviant sound independently of the adaptation to the standard



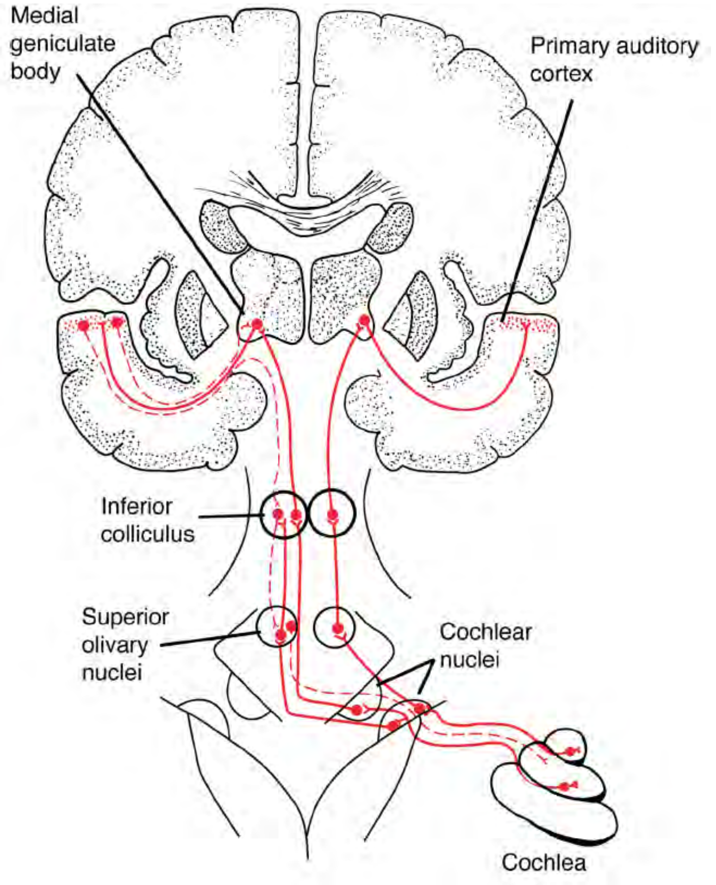


[Carbajal & Malmierca, 2018]
See also [Malmierca et al., 2015; Fong et al., 2020; Lesicko et al., 2022]

[Fong et al., 2020]

Deviance detection in the mature auditory system

- Deviance detection was described in the **auditory cortex, medial geniculate body (MGB) and inferior colliculus (IC)**. It has not been found in the cochlear nucleus.
- Studies have characterized deviance detection in adult mice, gerbils, guinea pigs, cats, songbirds, big brown bats, and macaques under an **anesthetized or awake state**.
- Deviance response depends on **tuning field properties** of the neurons.
- Deviance responses changes with oddball **protocol parameters**. It has been observed as a response to **pure tones**, but also to **white noise**, **tone clouds** and **vocalization**.



Adapted from [Patel, A. D., 2011]

[Ulanovsky et al. 2003; Malmierca et al. 2009; Antunes et al. 2010; Malmierca et al. 2018; Malmierca et al. 2009, Antunes et al. 2010, Nelken et al. 2014 and 2021, Zhai et al. 2019, Harpaz et al. 2021, Nelken et al., 2021, Lesicko et al., 2022, …]

1. How is deviance response changing during juvenile development?
2. How does experience influence this development?
3. What neuronal circuits underlie the changes in deviance response?

Patricia Valerio

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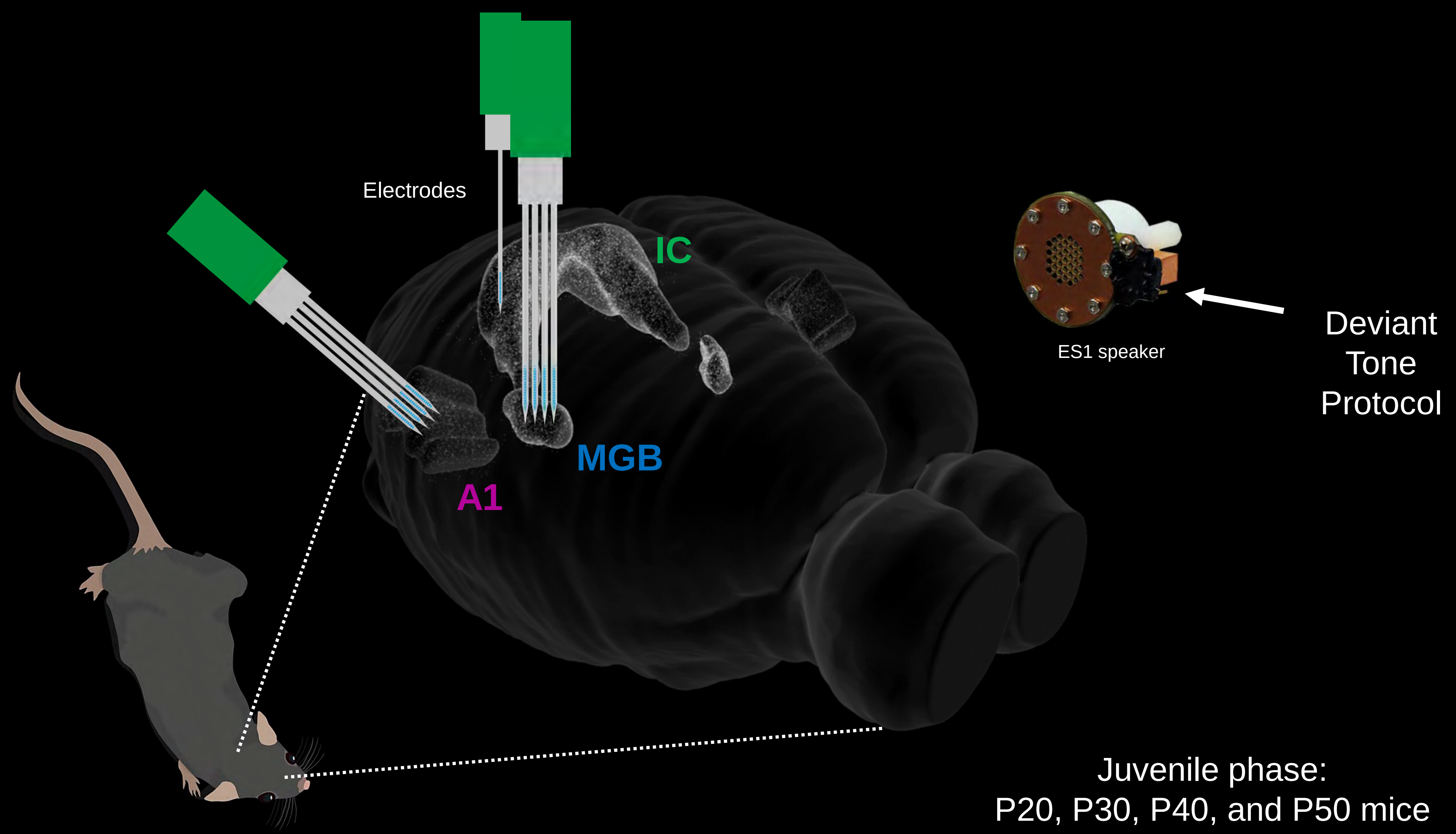
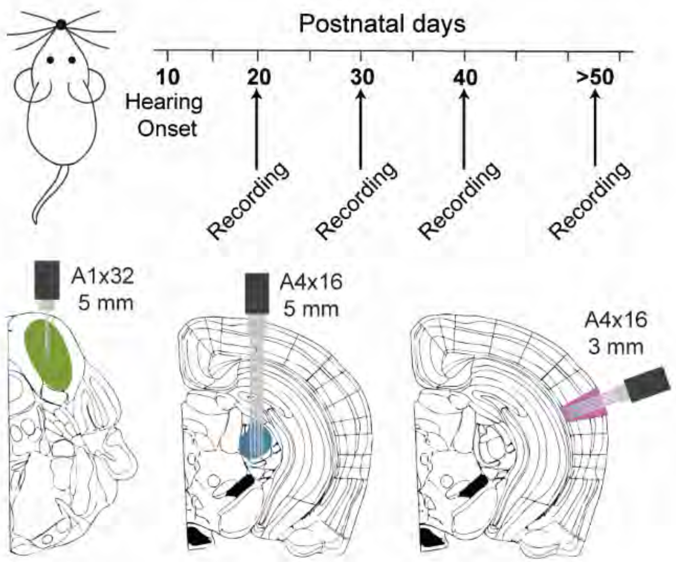
Patricia Valerio

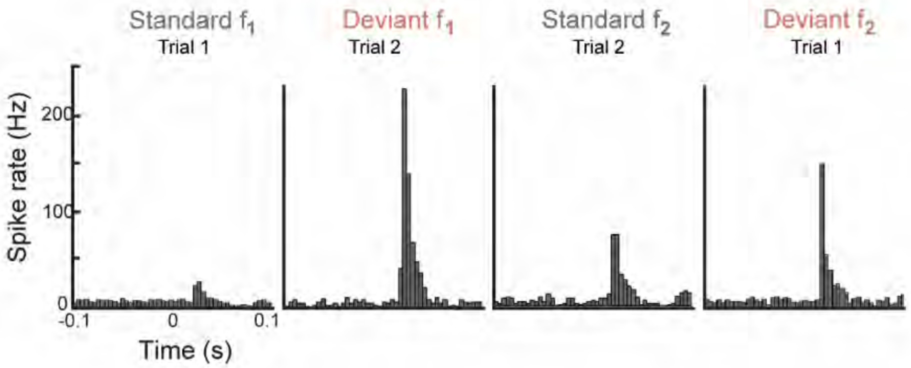
Electrophysiological recordings in awake mice

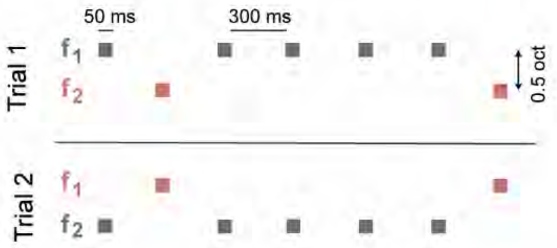


EPFL Blue Brain Cell Atlas

Deviance detection is quantified through comparison of standard and deviant responses







10 sequences - 1 to 10 standards (ST) preceding 1 deviant (DT)
15 repetition of each sequence in randomized order

Surprise Index

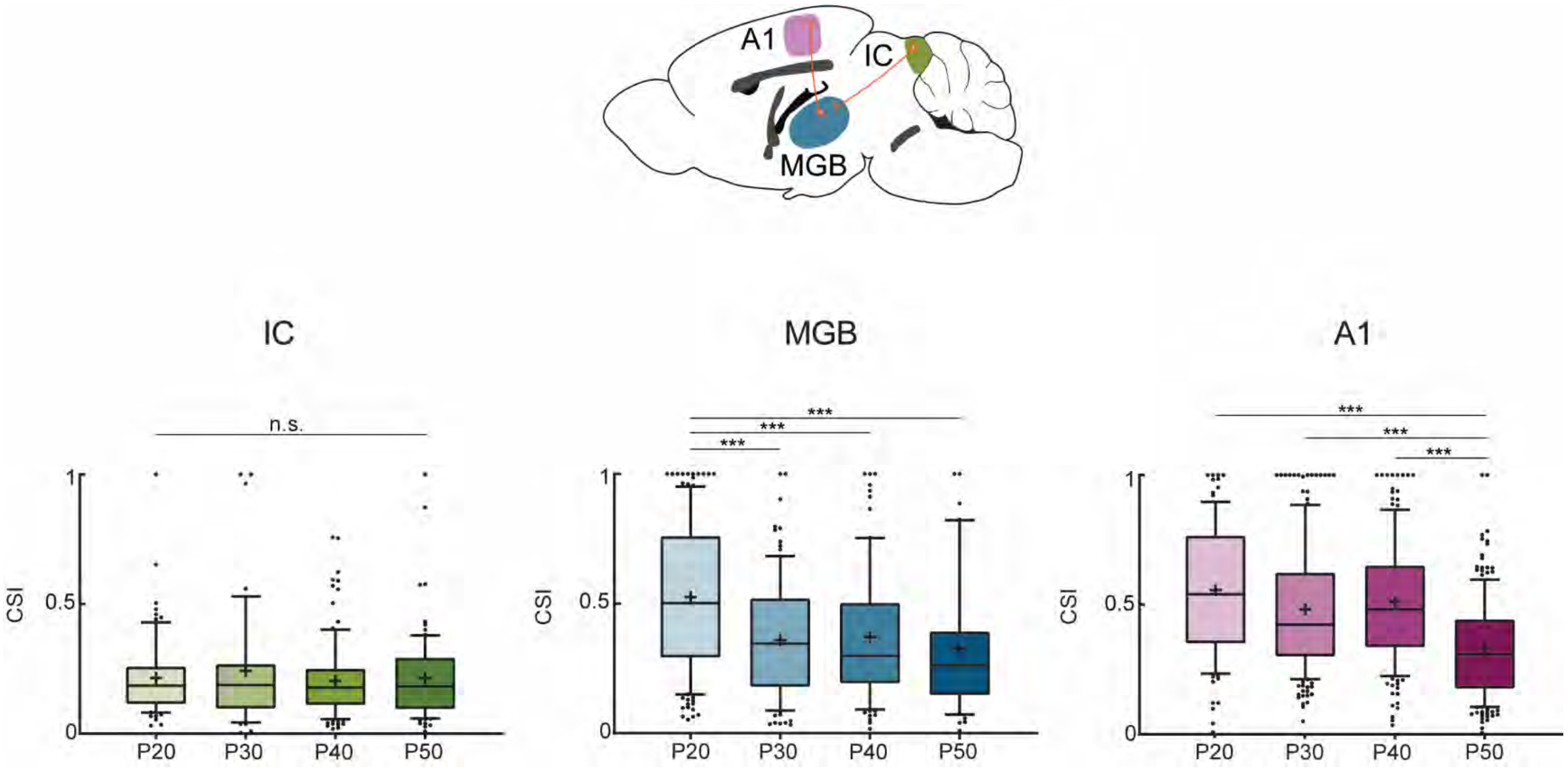
$$SI\ (f_i) = \frac{DT(f_i) - ST(f_i)}{DT(f_i) + ST(f_i)}$$

Combined surprise Index

$$CSI = \frac{DT(f_1) + DT(f_2) - ST(f_1) - ST(f_2)}{DT(f_1) + DT(f_2) + ST(f_1) + ST(f_2)}$$

DT, ST: evoked spike rate in 0-60 ms

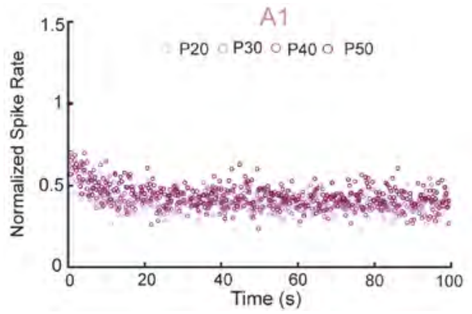
Deviance responses matures sequentially along the central auditory system



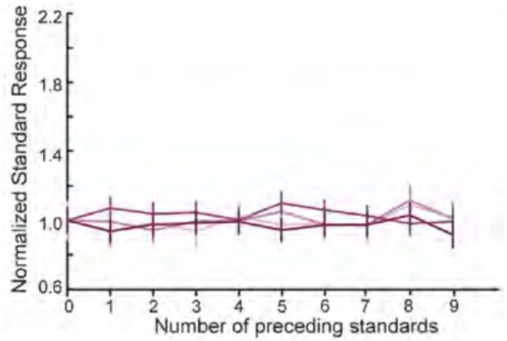
Deviance detection maturation depends on the response to the deviant but not to the standard tone

We showed that deviance detection maturation is independent of:

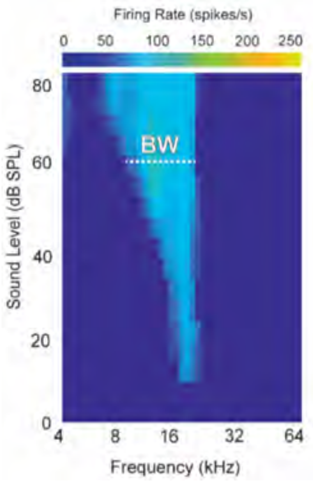
- Changes in adaptation to the tones across adolescence



- Changes in responses to the standard tone across adolescence



- Functional properties of neurons in response to pure tones
  (i.e. BW, threshold etc)



1. How is deviance response changing during juvenile development?
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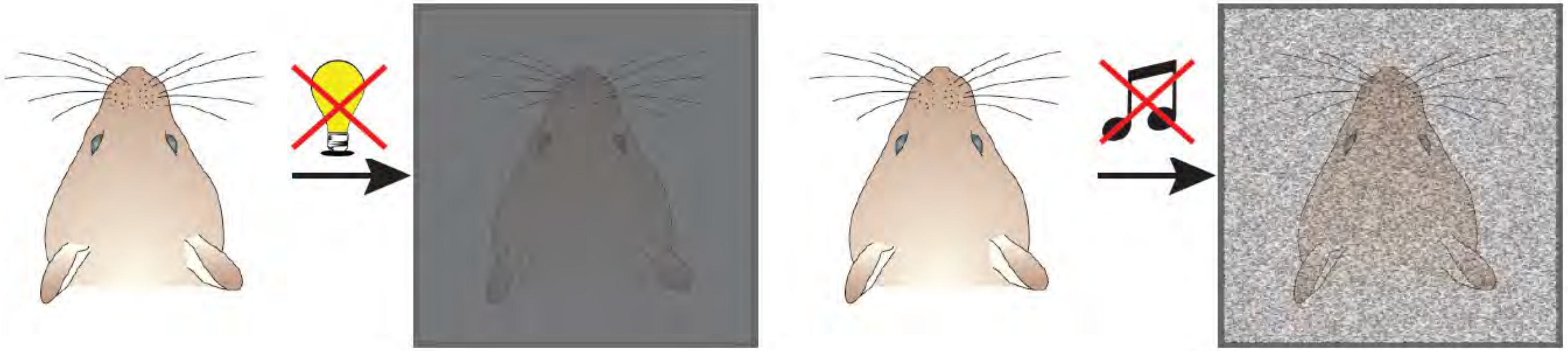
Masking sensory inputs

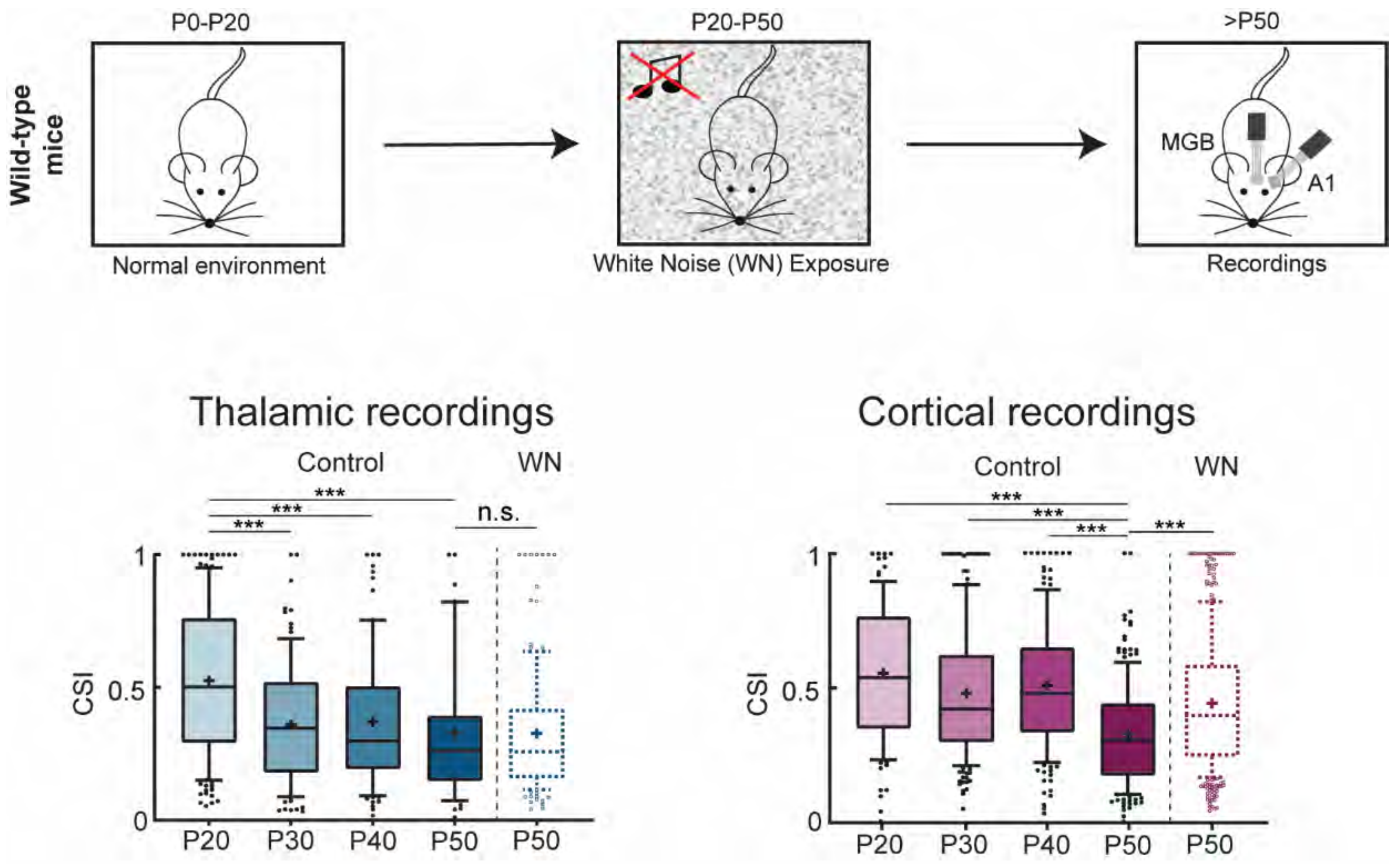
In the visual system:
Dark Rearing

In the auditory system:
White Noise Exposure



[Speechley et al., 2007]
[Nakamura et al., 2020]

Auditory experience affects deviance detection maturation in cortex, but not in thalamus



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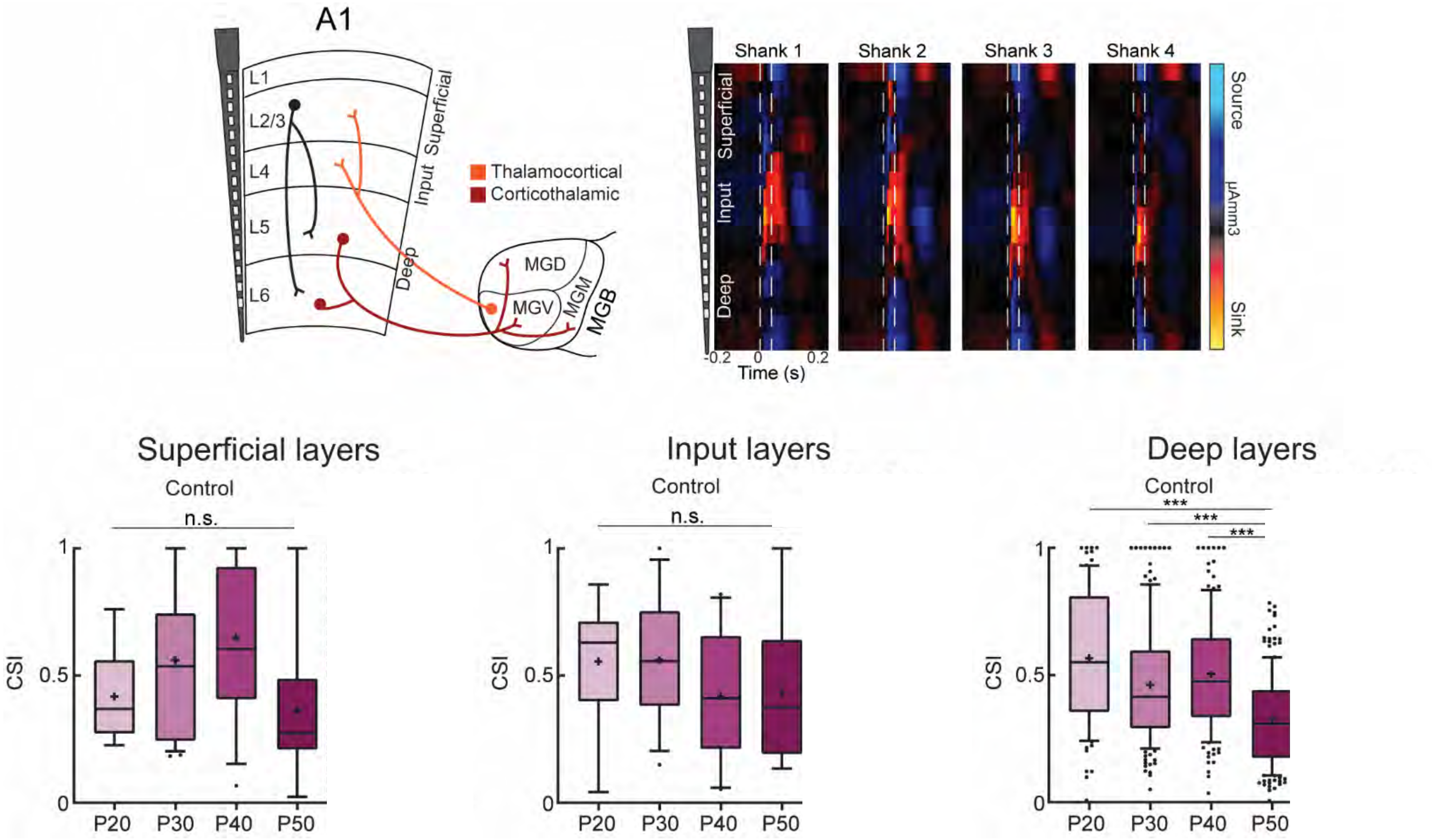
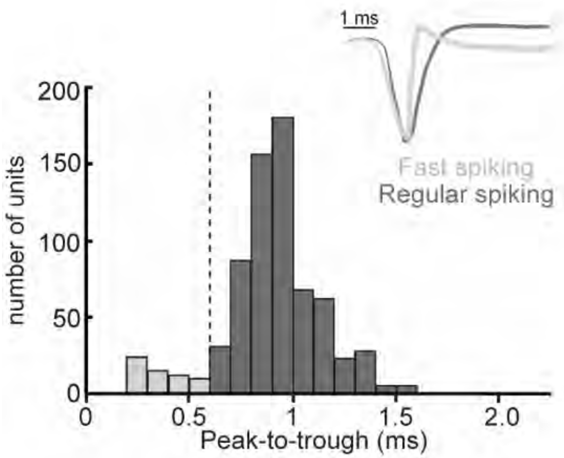
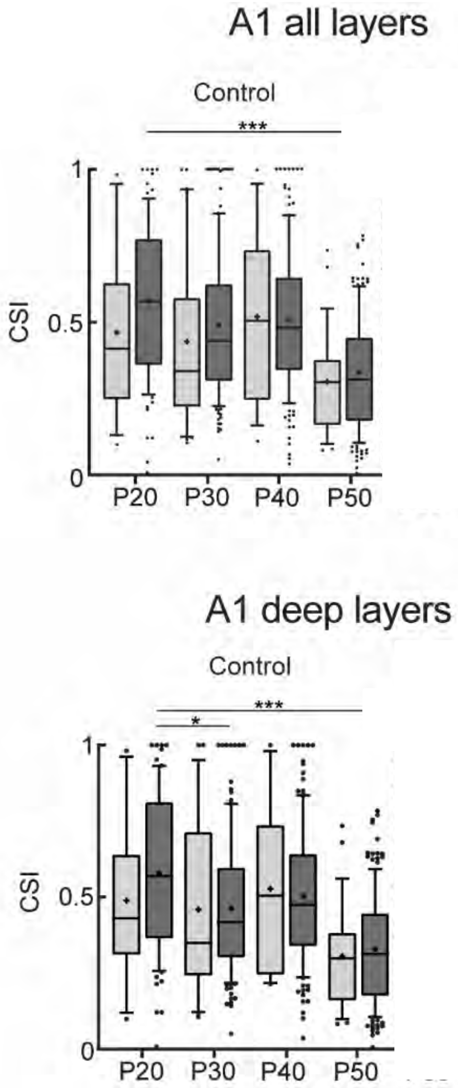
A1 deviance detection maturation is specific to deep layers



A1 deviance detection maturation is similar in regular and fast spiking neurons





Implication of corticofugal projections in deviance detection

Corticocollicular

Lesicko et al., 2022

Optogenetic (light) ACx inhibition

SSA is **not ablated** in IC, but levels are **decreased**

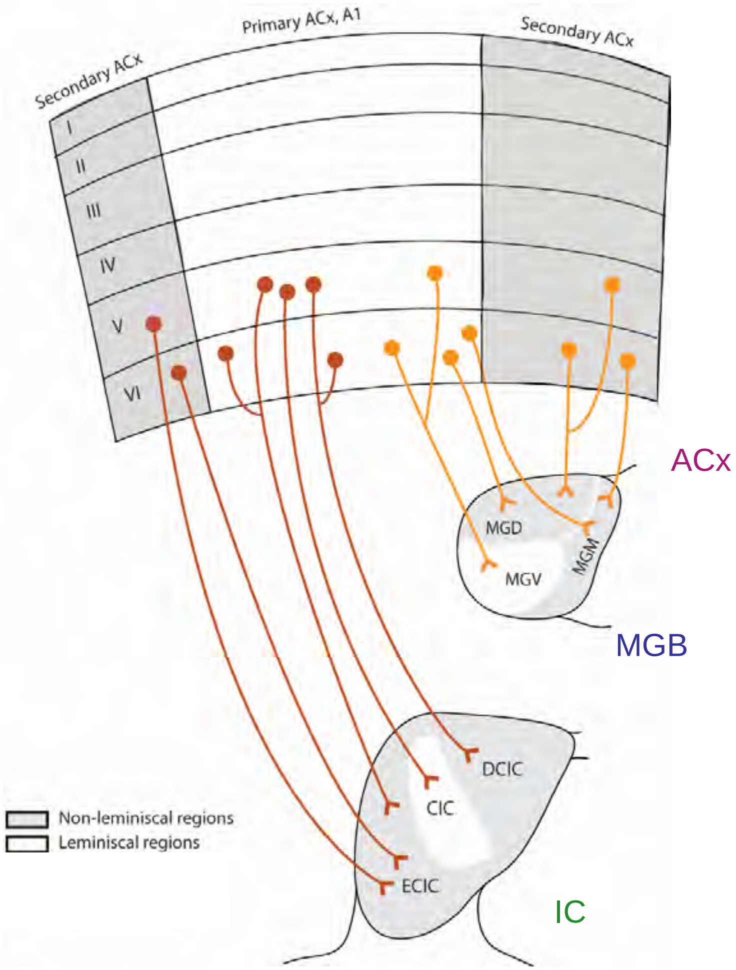
Conclusion: ACx does not generate SSA in IC, but might modulate it

Malmierca et al. 2013

ACx inactivation by muscimol

SSA is **not eliminated** in IC

Conclusion: ACx is not essential for the generation of subcortical SSA, but might modulate it



DCIC: Dorsal IC, CIC: Central IC, ECIC :External IC,
MGD: Dorsal MGB, MGM: Medial MGB, MGV: Ventral MGB

Adapted from [Malmierca, M.S. et al., 2015]

Corticothalamic

Malmierca et al. 2011

ACx deactivation by cooling

SSA remains **intact in MGB**

Conclusion: ACx is not required for generation of SSA in MGB, but might regulate it.

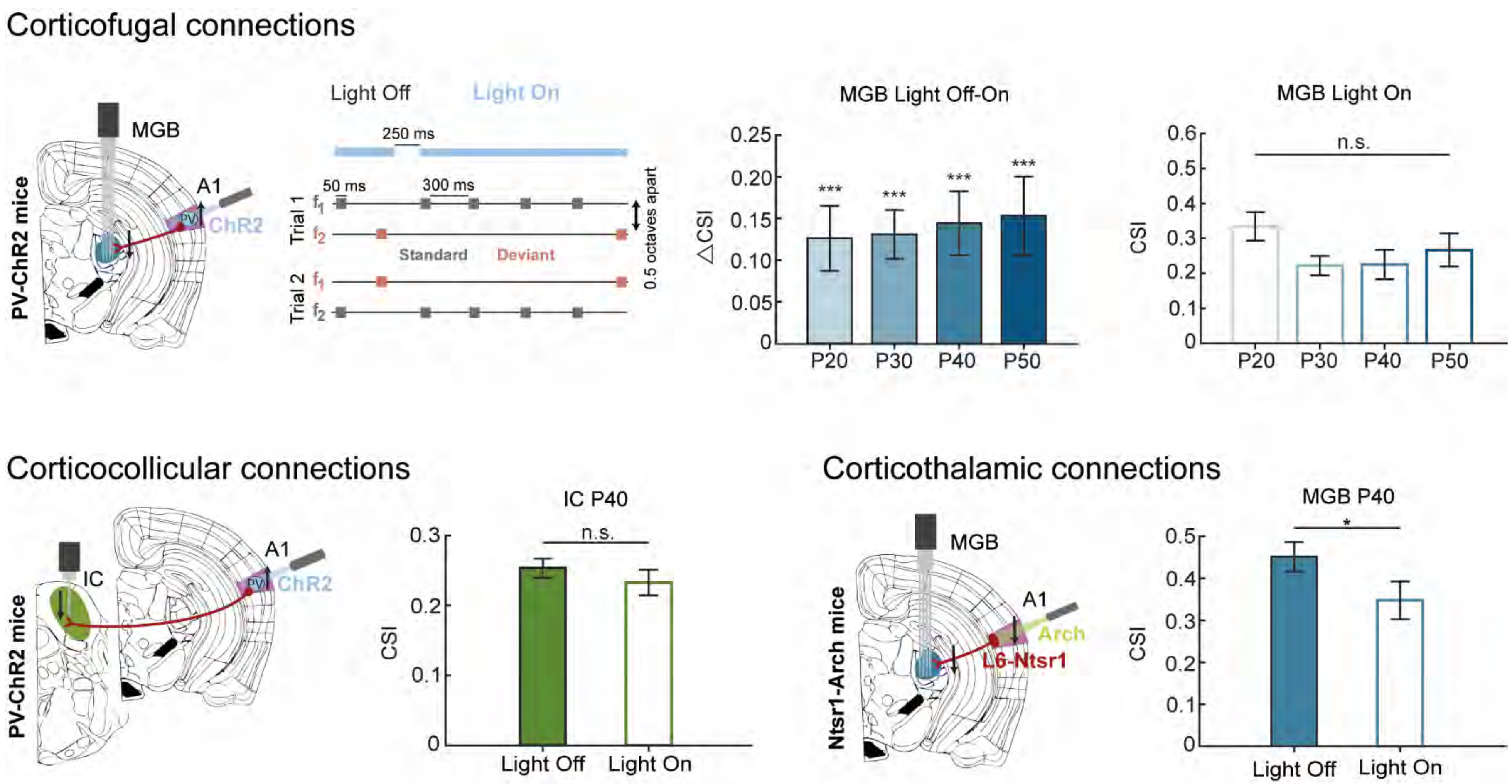
Gaese et al. 2011

ACx inactivation by muscimol

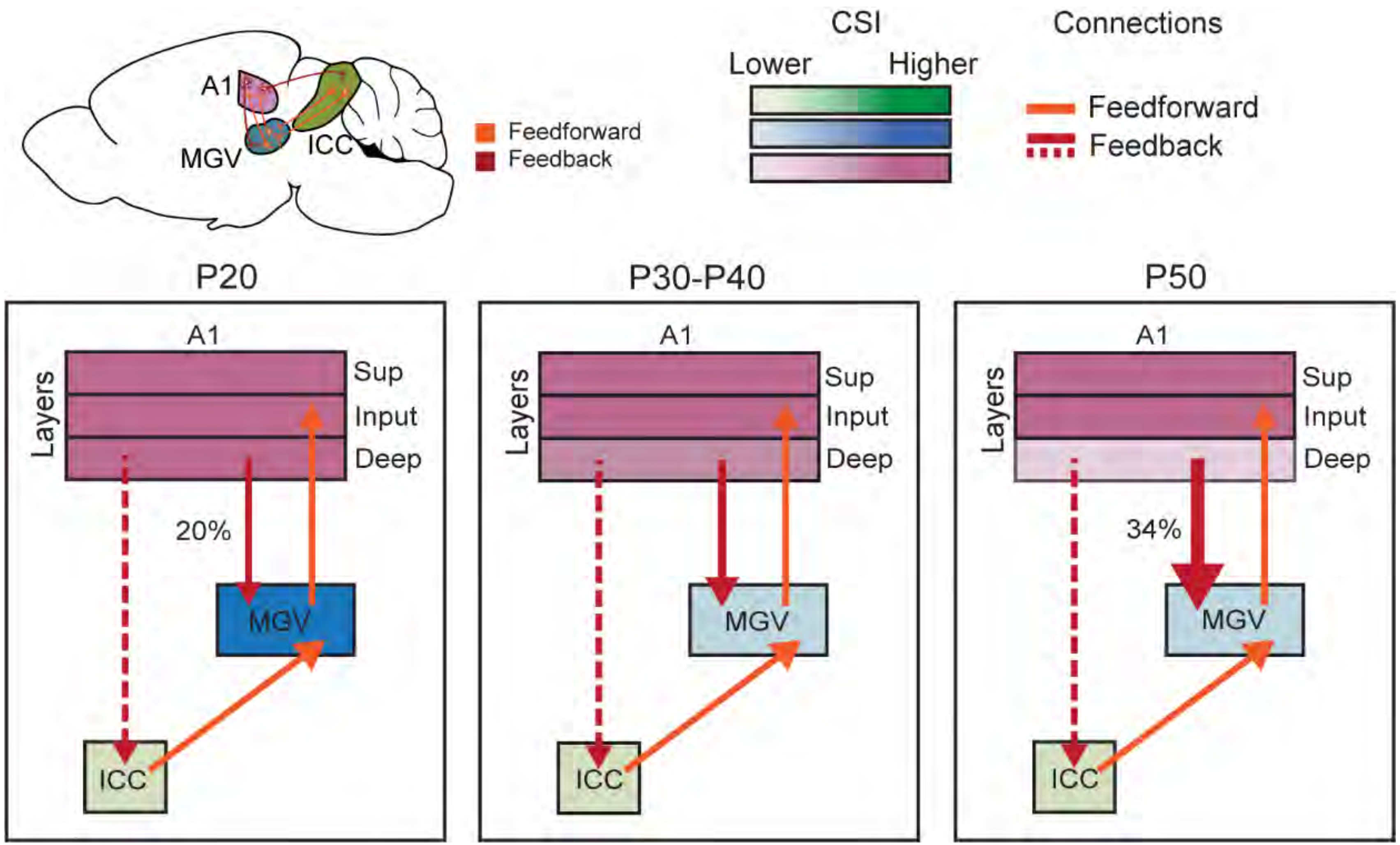
SSA **decreases** in vMGB

Conclusion: SSA in vMGB is mainly regulated by the corticofugal system

Corticothalamic projections are implicated in deviance detection maturation



Deviance detection across juvenile development



[Valerio et al., 2024]

Maturation of deviance detection across the central auditory system is sequential.

Maturation of deviance detection is experience-dependent in A1, but not in MGB.

The developmental approach allows dissecting the many circuits involved in deviance detection.

Patricia Valerio

Florian Studer
Sebastian Reinartz
James Taylor
Maria Shujah
Tommaso Zeppillo
Irenäus Stec
Mari Nakamura
Nicole Schütz

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