NETHERLANDS INSTITUTE FOR NEUROSCIENCE
Master the mind

VU VRIJE UNIVERSITEIT AMSTERDAM

Effect of early visual experience on audiovisual processing in mouse visual cortex

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Multisensory Integration

- unimodal stimuli can be **enhanced or suppressed** by pairing with another modality (**MI**)
- **MI** most useful for <u>detecting</u> weakly effective stimuli - **inverse effectiveness**
- **MI** largely absent at birth & **experience-dependent**
- **impaired after vision restoration** in individuals **born** with dense bilateral **cataracts**
- mostly studied in humans and cat Superior colliculus (a bit in mouse V1)
- **<u>single-neuron-level across visual areas unmapped</u>**

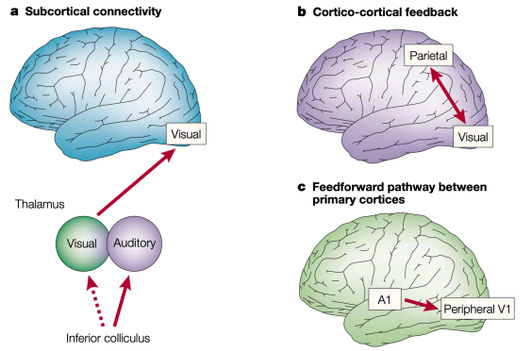
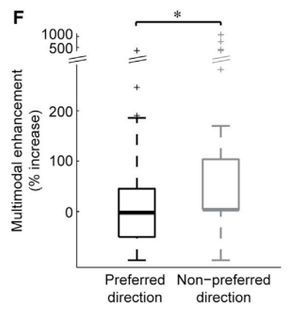


Figure 1 | **Possible mechanisms at the system level for cross-modal plasticity.**

Bavelier & Nevile (2002)

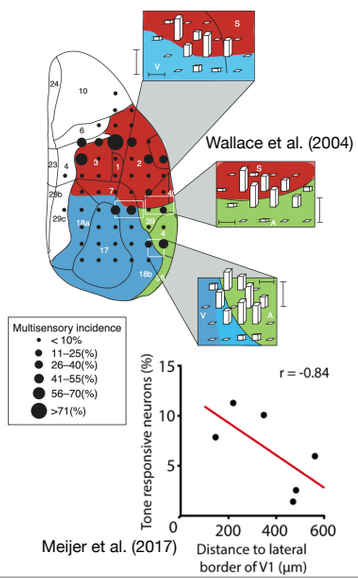


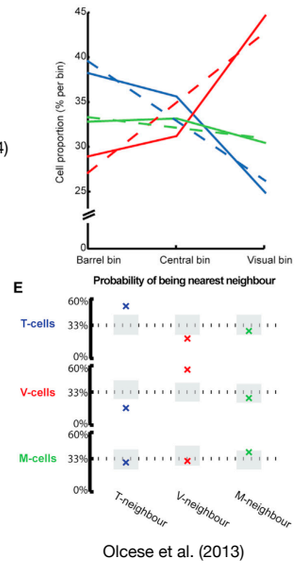
Olcese et al. (2013)

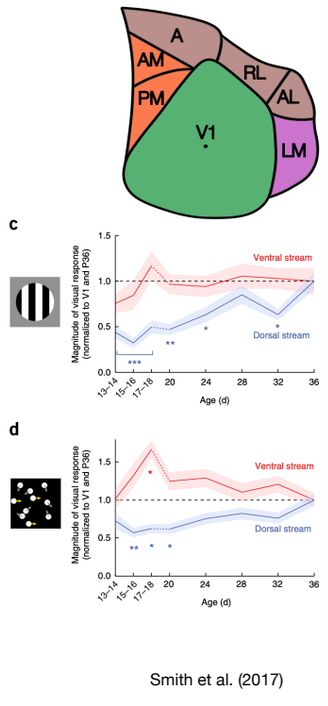
a) SUBCORTICAL In blind mole rats, there is evidence that the inferior colliculus, an auditory relay, projects not only to the part of the thalamus that is auditory, but also to the visual thalamus, resulting in the recruitment of the non-degenerated visual cortex by auditory stimuli. Similar changes might occur in the case of hereditary blindness (or deafness), allowing visual areas (or auditory areas) to be recruited for auditory (or visual) processing
b) ASSOCIATION -> PRIMARY
c) PRIMARY -> PRIMARY

Multisensory Integration: WHERE?

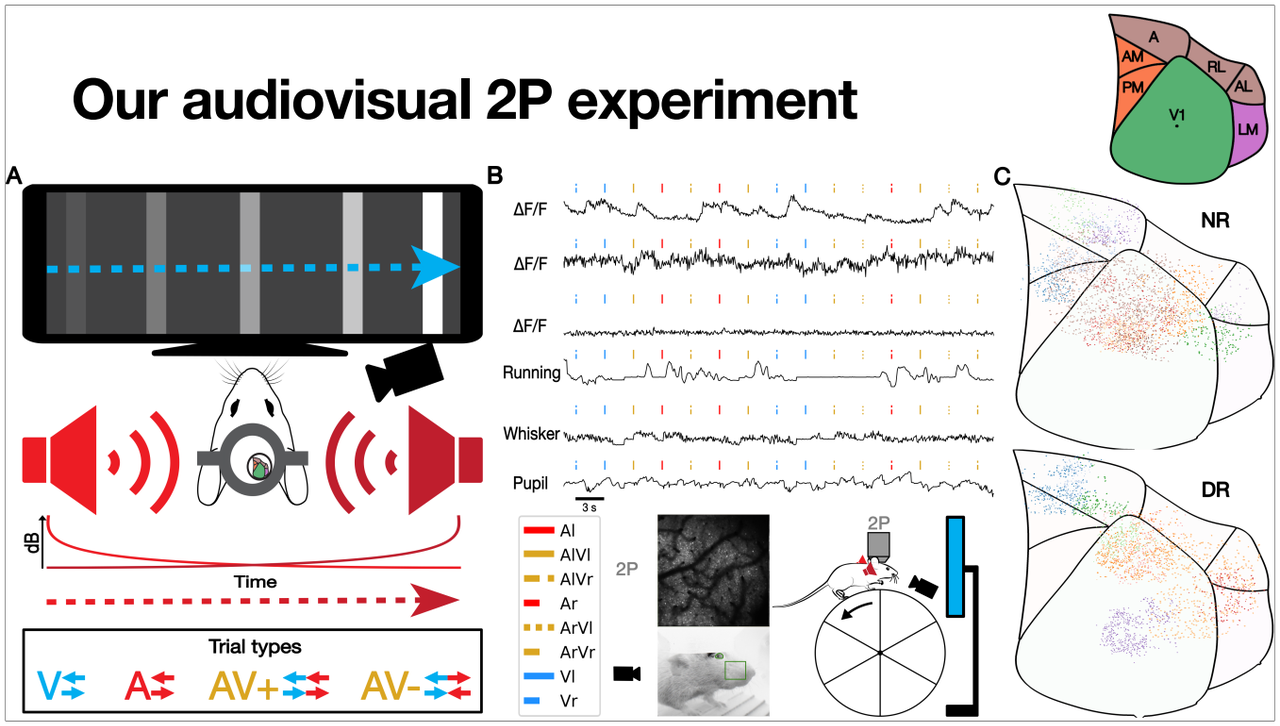
- **MI** assumed highest in **border regions**
- in **RL** evidence of **clustering** of **unimodal cells** (visual and tactile)
- **<u>Dorsal vulnerability hypothesis</u>**





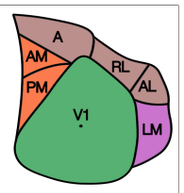


example in RAT, (closer to other modality sensory region, more MI)
rodent V1 visual neurons with different feature tuning mixed (although local connectivity feature specific)



initial idea was to investigate congruency-based AV integration

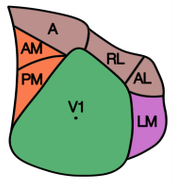
Hypotheses



- Shift in balance towards auditory processing and away from visual processing
- Auditory responses enhanced, visual responses weakened in dorsal stream
- Multisensory integration affected in dorsal stream
- Congruent enhanced (stimulus detection), Incongruent enhanced (PP)
- Auditory gradient towards lateral side, more nonvisual neurons in HVAs
- Clustering of unimodal neurons (maybe disrupted by DR?)

initial idea was to investigate congruency-based AV integration

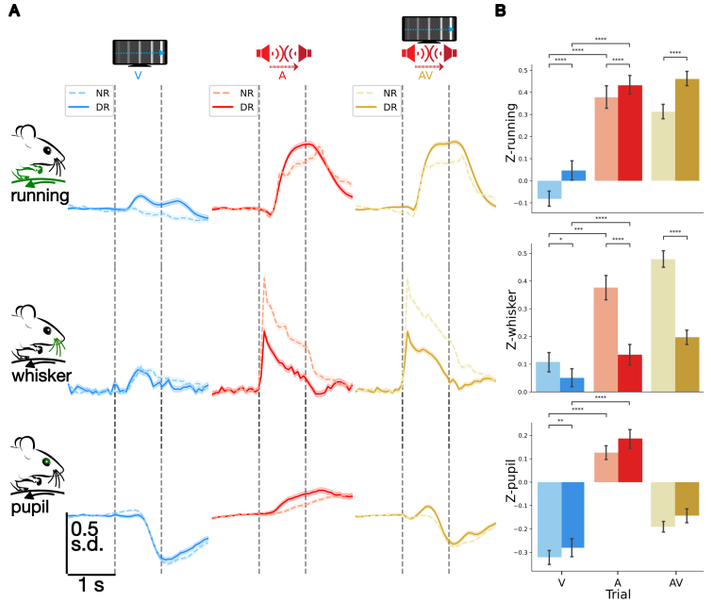
Hypotheses **vs <u>Outcomes</u>**



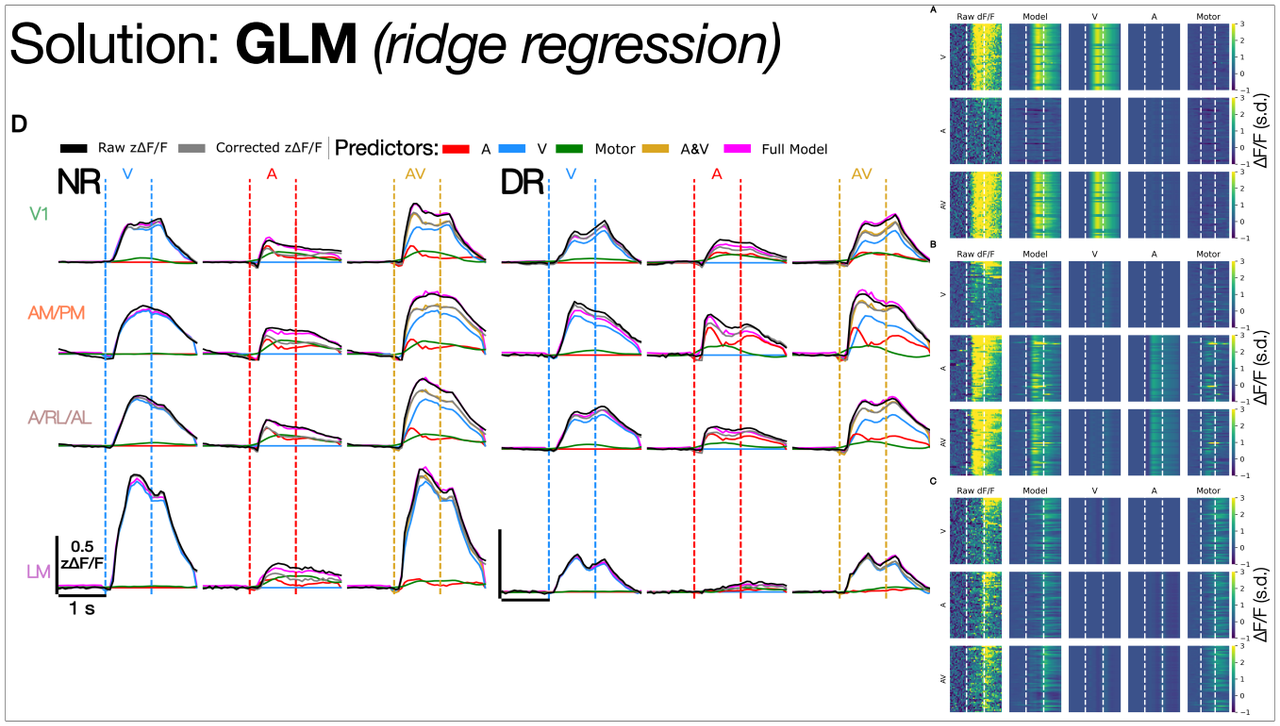
- **Shift in balance towards auditory processing and away from visual processing**
- <u>Auditory responses enhanced, visual responses weakened</u> in **dorsal stream (+ V1)**
- <u>Multisensory integration affected</u> in **dorsal stream (+ V1)**
- ~~Congruent enhanced (stimulus detection), Incongruent enhanced (PP)~~
- ~~Auditory gradient towards lateral side~~, <u>more nonvisual neurons</u> in **HVAs (+ V1)**
- ~~Clustering of unimodal neurons~~ (**<u>maybe affected</u> by DR**?)

initial idea was to investigate congruency-based AV integration

Problem: **Systematic differences in stimulus-evoked movements between DR and NR mice**



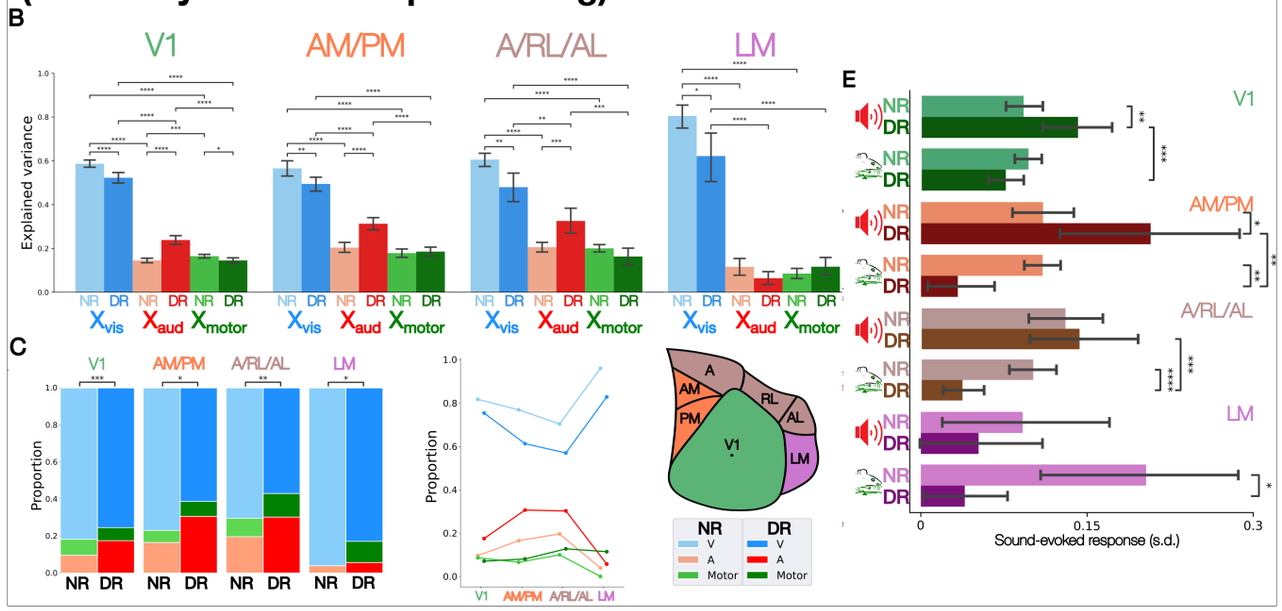
BIG problem because we want to claim differences between groups but our confound differs between groups



VISUAL top neuron : LM
AUDITORY middle neuron: V1
MOTOR bottom neuron: A/RL/AL

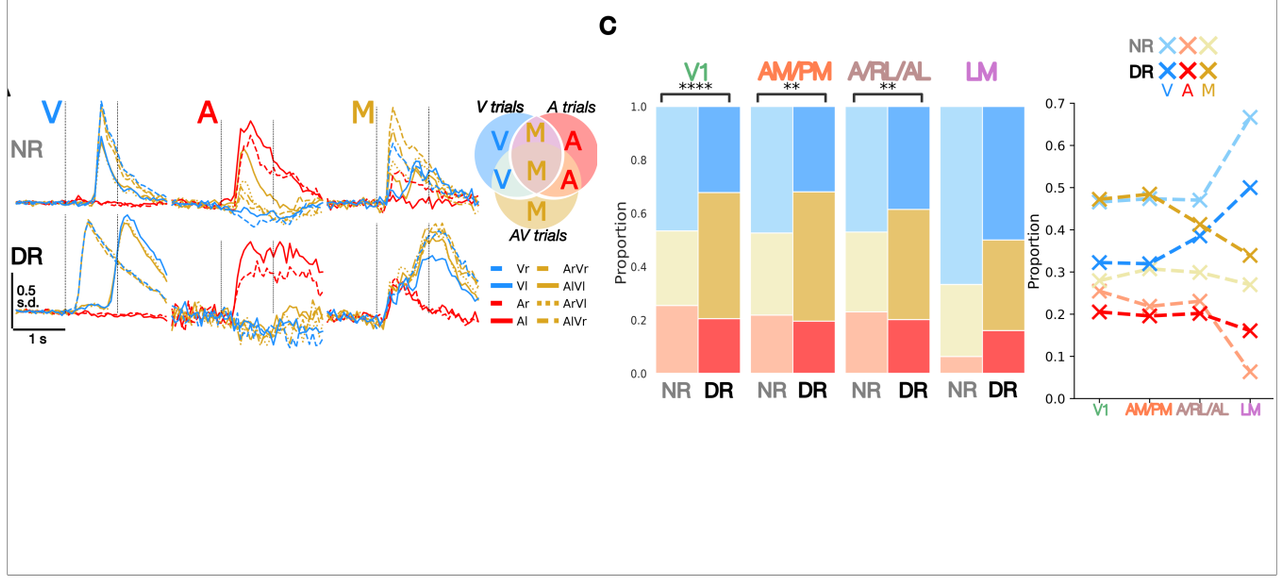
Dark rearing induces shift towards auditory processing

(and away from visual processing)

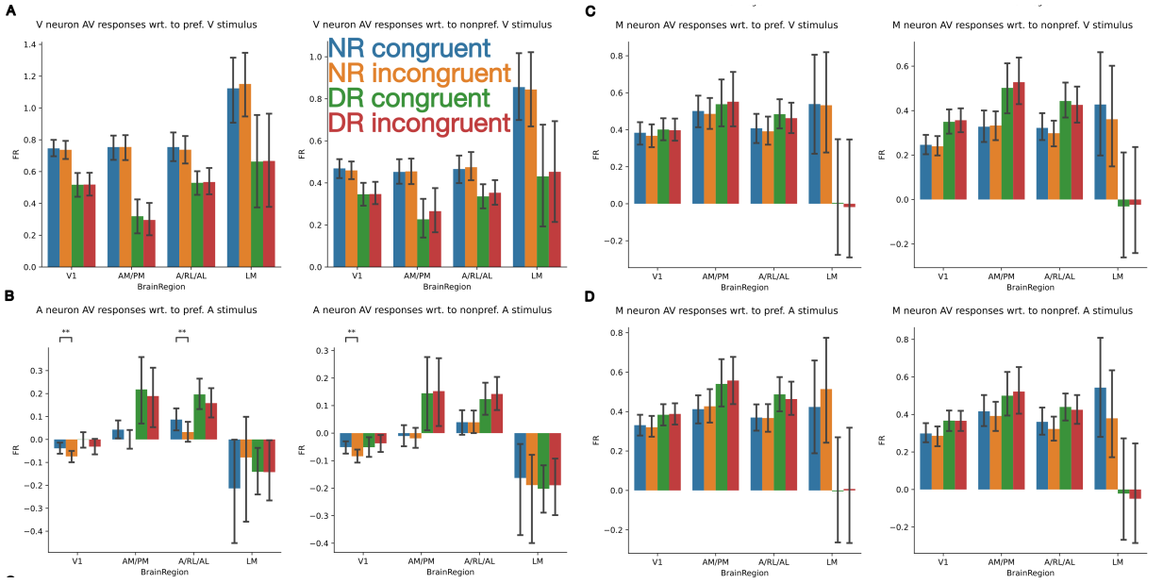


Dark rearing induces shift towards auditory processing

(and away from visual processing) - *CONTINUED*



~~Congruent vs Incongruent AV trials~~



no diff so GROUP!

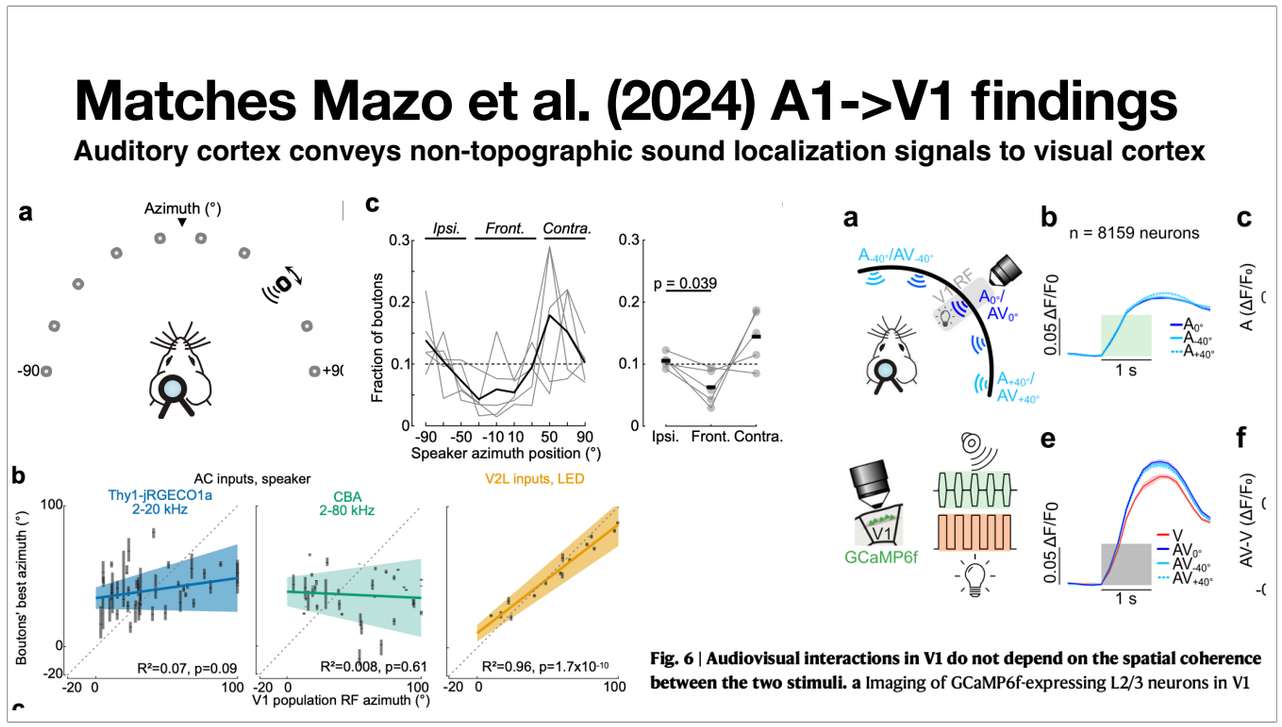
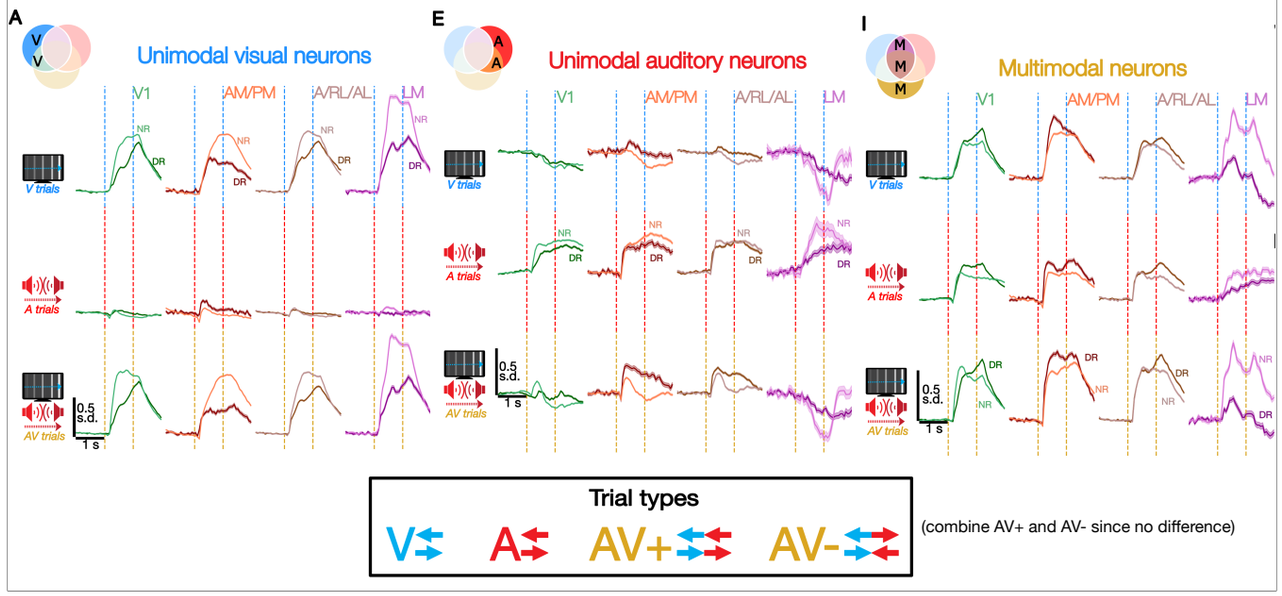


Fig. 6 | Audiovisual interactions in V1 do not depend on the spatial coherence between the two stimuli. a Imaging of GCaMP6f-expressing L2/3 neurons in V1

does not mean that sound location cannot be decoded (I didn't do it but would be really key to do in my opinion, would expect better decoding in DR)

very clear decodable information about sound location, just not retinotopically mapped
includes basically equally represented inputs about sound location in contralateral hemisphere
in contrast SC and IC there the maps are aligned (important for localization)

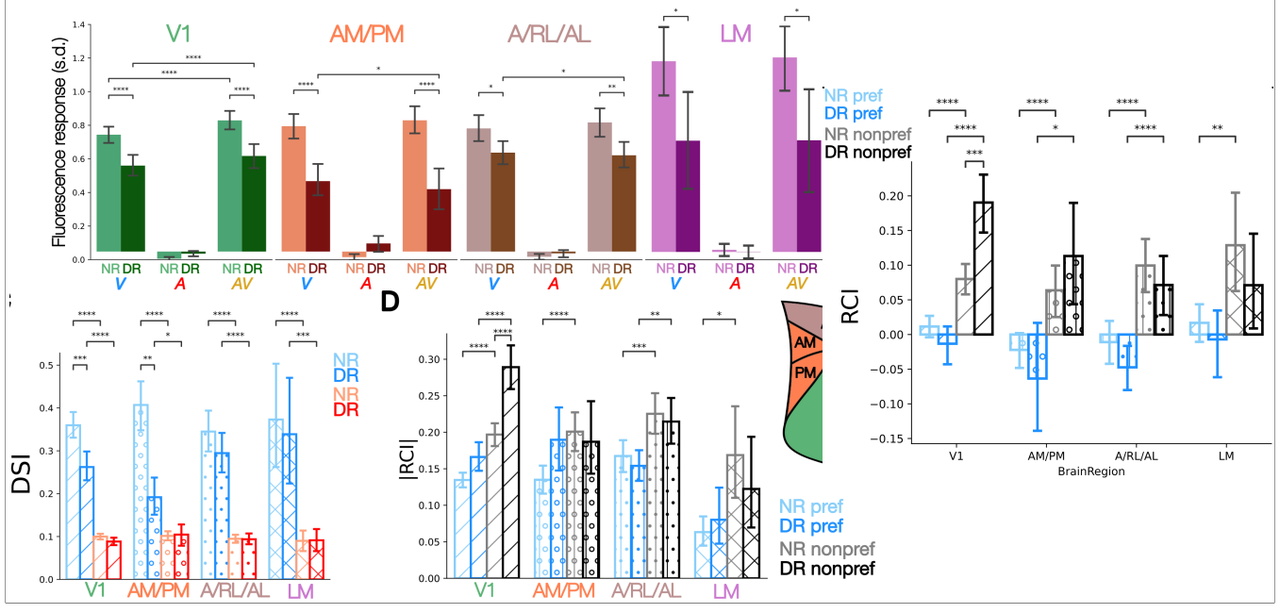
Average stimulus-evoked responses across neuron types and trial types



we combine AV+ and AV- and just look at AV trials

it makes sense now that neurons might have a clear auditory receptive field (or even direction preference) but the visual receptive field and direction preference of the same neuron might be completely different, since no clear correspondence between the 2

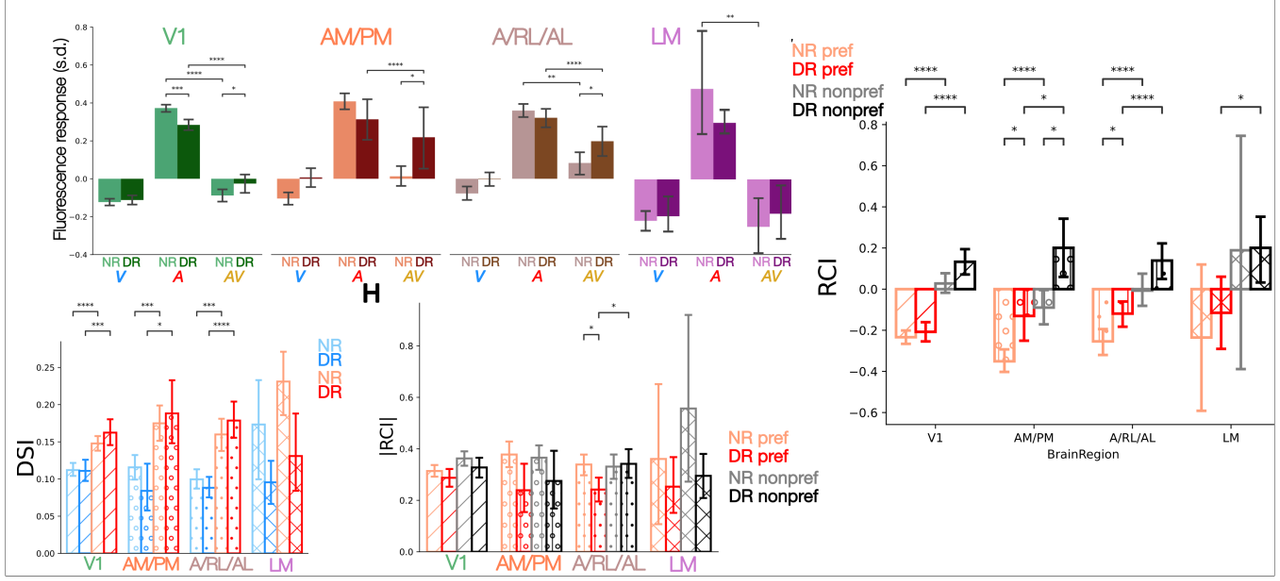
Weakened visual responses, direction selectivity and enhanced V1 MI in unimodal visual neurons of DR mice



that nonpreferred stimuli more enhanced is inverse effectiveness
in NR consistent with the idea that balance ~50/50 between excitation and inhibition in V1 (Guido). seems to differ across areas and also between DR and NR a bit (not shown but overlapping CI)
for preferred stimuli, mostly suppression (suppressed with sound vs without)

vs for nonpreferred stimuli (to enhance detection) generally enhanced also in NR
somehow this is selectively enhanced in DR V1 (although even MI for preferred visual stimuli seems close to significant for DR V1 and DR AM/PM)

Enhanced audiovisual responses and altered MI in dorsal stream unimodal auditory neurons in DR mice

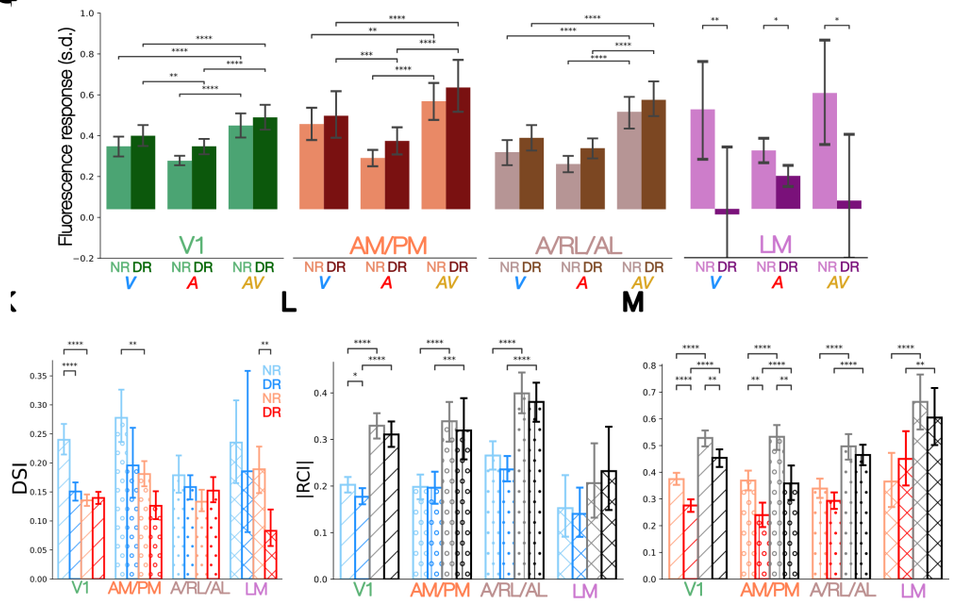


DSI stronger for auditory than visual stimuli

across the board unimodal aud predominantly supressed in NR. while become a bit more enhanced for nonpreferred, this is really much more pronounced for DR in dorsal stream

whereas the "normal" suppression is less pronounced in DR compared to NR

Weakened direction selectivity and multisensory integration in multimodal neurons of DR mice



these are the neurons that actually perform MI (basically mostly response enhancement)
MI differences really in how preferred sound directions enhanced by pairing with vision! (in both preferred and nonpreferred in V1 and dorsal stream)
not so much in how preferred bar directions enhanced by sound (although this is reduced in V1)

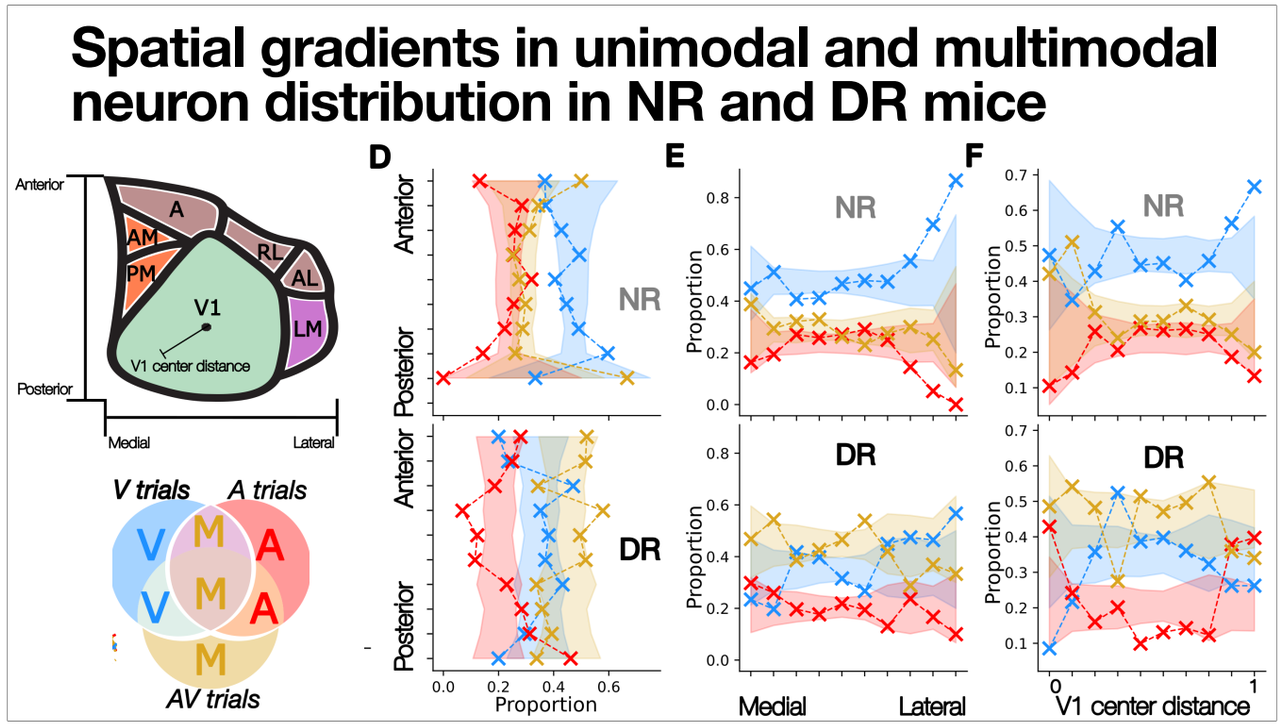
Discussion: Possible theoretical framework

Auditory inputs remain unpruned with lack of visual experience, shifting balance away from normal visual processing towards unrefined intermixing of auditory information

- Role of **unimodal neurons** is to mainly **convey information** about **their modality**, while **multimodal neurons** do **“integration"** of information from the **multiple modalities**
- With DR, **less unimodal visual** neurons **embedded** in a **more nonvisual environment**
- Different **balance** of **response enhancement** and **suppression** in MI of preferred and non-preferred stimuli:
  - **preferred**: do some **further processing / relay** of that information, **enhance multimodal** neurons, **suppress unimodal** neurons (both processes disrupted in V1 and dorsal stream of DR)
  - **non-preferred**: enhance **stimulus detection**, **enhance both unimodal and multimodal** neurons (in unimodal neurons this is excessive whereas in multimodal neurons it is reduced)
- When **congruency** of audiovisual input makes a difference:
  - **SC & IC** (contains **topographically mapped visual and auditory field** -> those **areas** evolved for **detection, localization, orienting**)
  - **V1** but **NOT location / direction!**, instead **frequency** vs spatial frequency, **loudness** & contrast! (A1 inputs to V1 are NOT topographically mapped)

Discussion: Future directions

- **More animals** to strengthen conclusions about **LM** and **AM/PM**
- **Decoding**; **manifold analysis** (using dPCA) - since **spatial location IS reliably encoded in A1 inputs** to V1, would be interesting to see **how** it is **represented** in the **population code** in different areas and how visual experience affects this
- **Isolating A1 inputs** by silencing / optogenetically stimulating; using different GECIs for A1 inputs
- To **identify the circuits** guiding **differences** in **response enhancement / suppression in V / A / M** functional **neuron types** need **modeling** and **patch** / **opto / DREADDs** data + find out **role of interneurons**
- **Different experiment** needed to tease apart **congruency effects** (frequency, loudness; might help distinguish V1 and dorsal stream)
- Where and how **subcortical** (thalamic, SC) **inputs to visual cortex fit** into the picture with the **V / A / M neuron types**
- **More directions / orientations / frequencies** would allow much **more thorough modeling and characterization** of the interplay between vision and audition
- Investigating **receptive fields in DR** on their own and in some of the current analyses
- **Chronic matching** to look at **recovery** AND whether **functional neuron types switch identity**! (eg. M -> V) and whether this happens more in DR or general phenomenon!

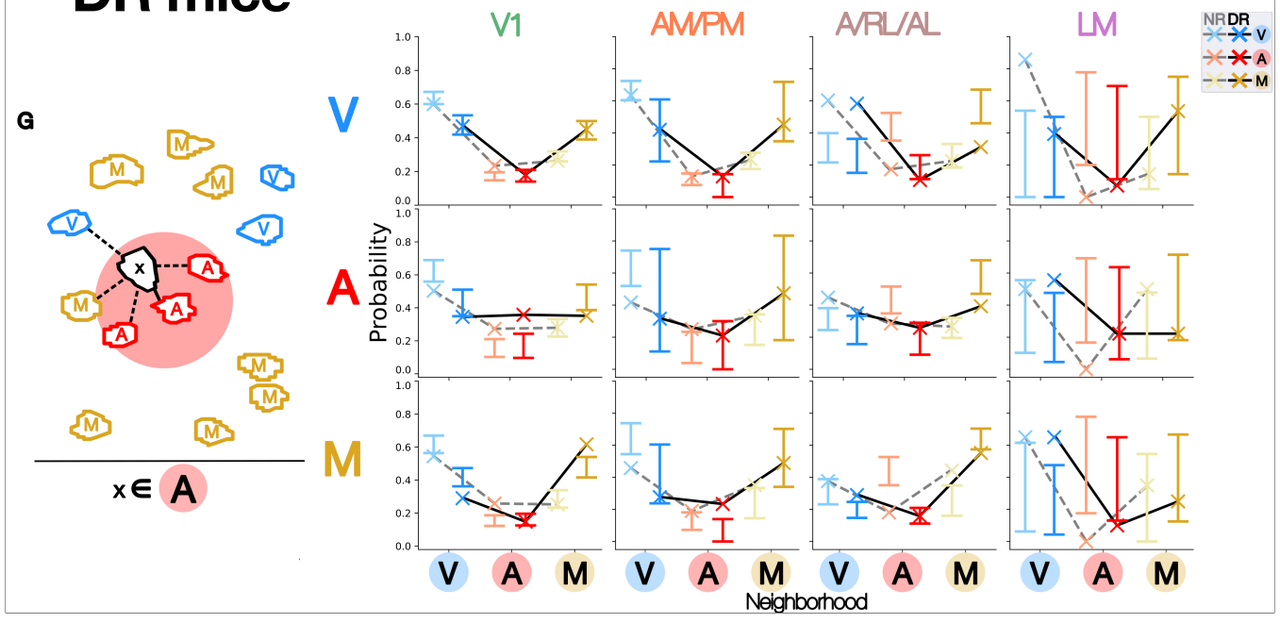


found opposite of expected. no gradient of auditory or multimodal neurons towards lateral side (but these are different auditory neurons we are considering anyways) - Guido only considered purple subset (negligible in our dataset)

more lateral areas include AL and LM which are by all means very visual; especially clear trend in NR but also in DR

MOST interesting,
DR neuron auditory concentration in center of V1 and also on the outside (suggests role for central V1 subpopulations of auditory cells as well as subpopulations in higher visual areas, but less so on the borders of V1 (contrary to expectation)

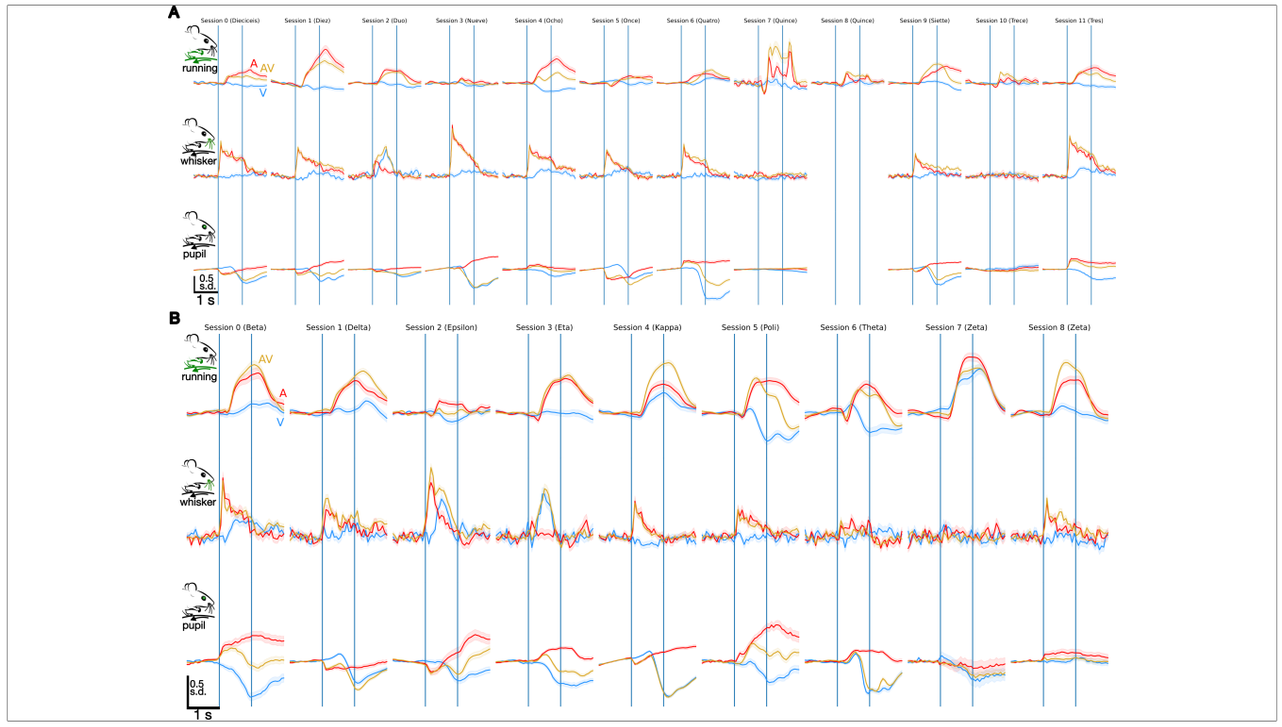
~~Clustering of unimodal neurons~~ affected in DR mice

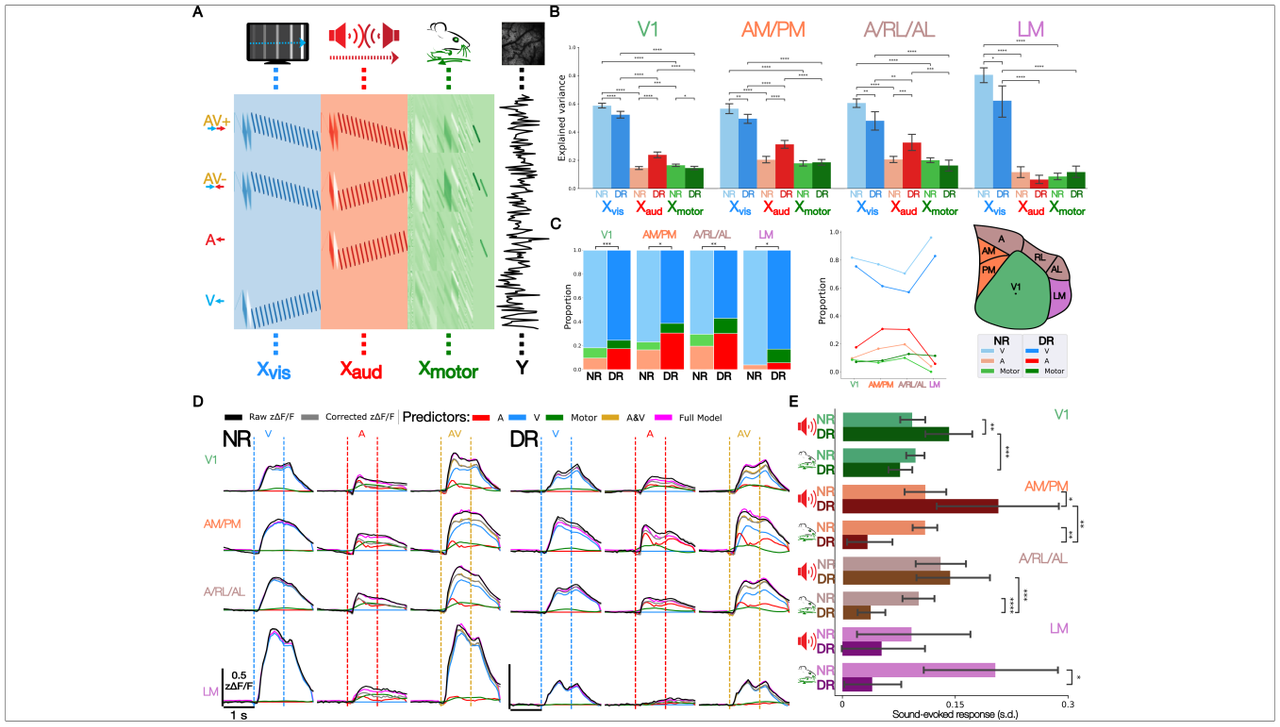


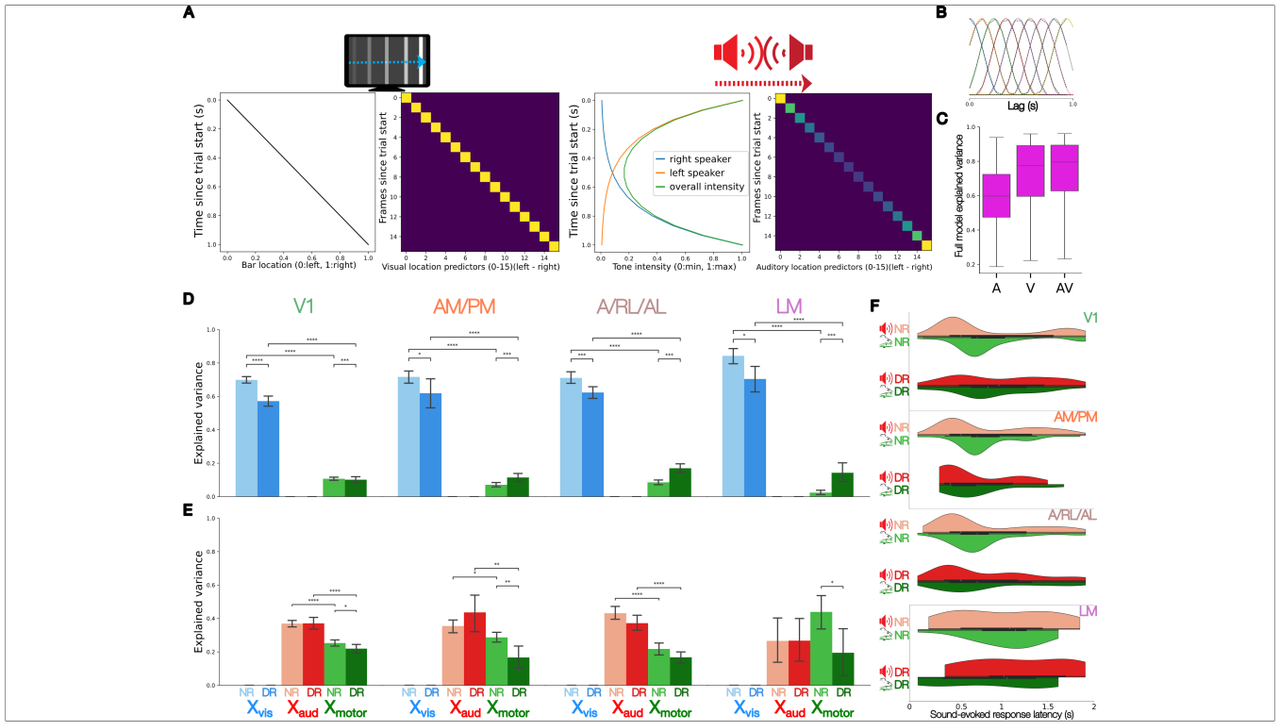
no clear clustering of unimodal neurons (in some regions and contexts, but not a general cortical trend; neither in NR nor DR)

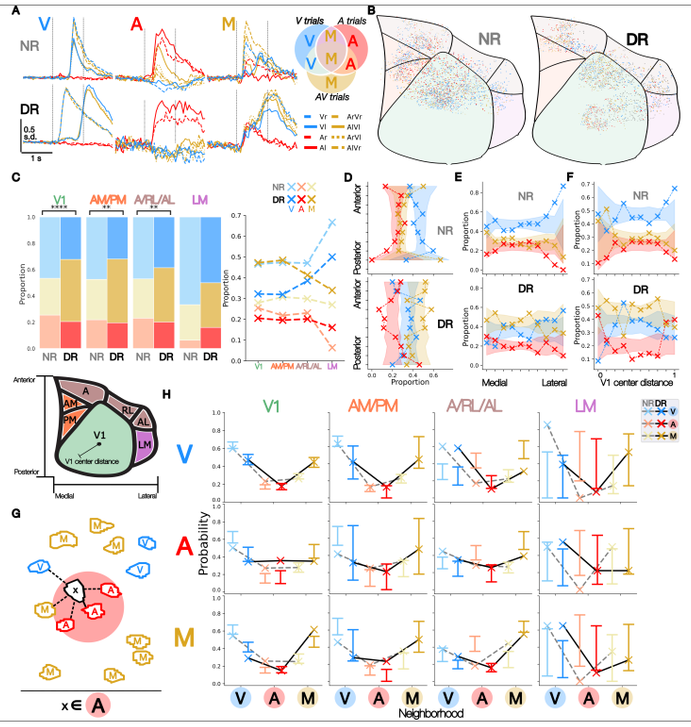
seems like diverse local neighborhoods are often beneficial (but in some cases clear clustering!

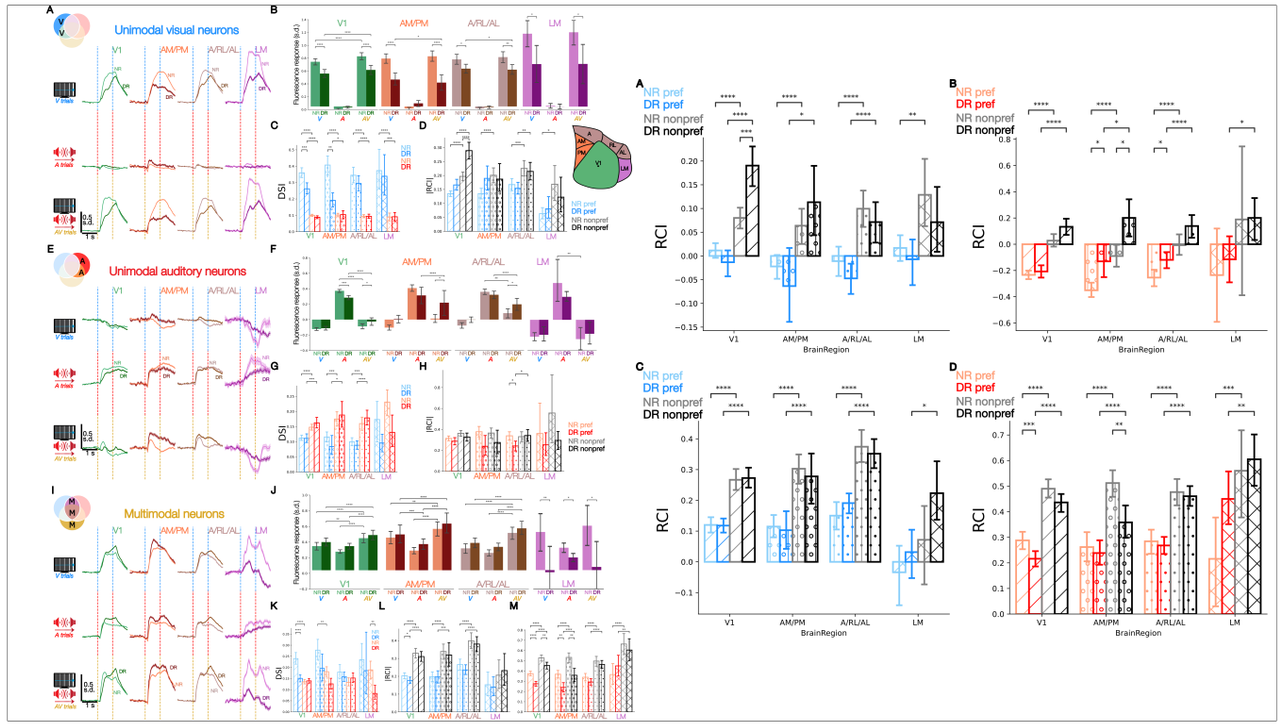
problem with very uneven proportion of neurons always dominated by V or M
still, differences between NR and DR are present


A
Session 0 (Diecieseis)
Session 1 (Diez)
Session 2 (Duo)
Session 3 (Nueve)
Session 4 (Ocho)
Session 5 (Once)
Session 6 (Quatro)
Session 7 (Quince)
Session 8 (Quince)
Session 9 (Siette)
Session 10 (Trece)
Session 11 (Tres)
running
whisker
pupil
A
AV
V
0.5 s.d.
1 s
B
Session 0 (Beta)
Session 1 (Delta)
Session 2 (Epsilon)
Session 3 (Eta)
Session 4 (Kappa)
Session 5 (Poli)
Session 6 (Theta)
Session 7 (Zeta)
Session 8 (Zeta)
running
whisker
pupil
AV
A
V
0.5 s.d.
1 s


A
B
C
D
E
V1
AM/PM
A/RL/AL
LM
Explained variance
NR DR NR DR NR DR
Xvis Xaud Xmotor
AV+
AV-
A+
V+
Xvis
Xaud
Xmotor
Y
Proportion
NR DR NR DR NR DR NR DR
V1 AM/PM A/RL/AL LM
A
AM
PM
RL
AL
LM
V1
NR DR
V
A
Motor
Raw zΔF/F
Corrected zΔF/F
Predictors:
A
V
Motor
A&V
Full Model
NR
DR
V
A
AV
0.5 zΔF/F
1 s
Sound-evoked response (s.d.)
0
0.15
0.3


A
Time since trial start (s)
Bar location (0:left, 1:right)
Frames since trial start
Visual location predictors (0-15)(left - right)
Time since trial start (s)
right speaker
left speaker
overall intensity
Tone intensity (0:min, 1.max)
Frames since trial start
Auditory location predictors (0-15)(left - right)
B
Lag (s)
C
Full model explained variance
A
V
AV
D
V1
AM/PM
A/RL/AL
LM
Explained variance
E
Explained variance
NR
DR
Xvis
Xaud
Xmotor
F
V1
AM/PM
A/RL/AL
LM
Sound-evoked response latency (s)


A
V
A
M
NR
DR
0.5 s.d.
1 s
V trials
A trials
AV trials
Vr
Vl
Ar
Al
ArVr
AlVl
ArVl
AlVr
B
NR
DR
C
V1
AM/PM
A/RL/AL
LM
Proportion
NR DR
D
Anterior
Posterior
E
Medial
Lateral
F
V1 center distance
G
x∈ A
H
Probability
Neighborhood


A
Unimodal visual neurons
V1
AM/PM
A/RL/AL
LM
V trials
A trials
AV trials
0.5
0.5
1 s
B
Fluorescence response (s.d.)
NR DR
V
A
AV
C
DSI
NR pref
DR pref
NR nonpref
DR nonpref
D
|RCI|
E
Unimodal auditory neurons
F
G
H
I
Multimodal neurons
J
K
L
M

A
NR pref
DR pref
NR nonpref
DR nonpref
RCI
V1
AM/PM
A/RL/AL
LM
BrainRegion
B
C
D