Anatomic and Physiological Basis of Clinical Tests of Otolith Function

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DISCOVERY OF MUSCLE RESPONSE TO SOUND

- Von Bekesy 1935 with 134 dB animals turn heads to loud sound by muscle reflex
- In 1964, Bickford, Jacobson, Cody first found EMG evidence of acoustically generated responses at the inion (neck/posterior skull)
- In 1971, Towsend found that the origin of the neck response at the inion was the saccule

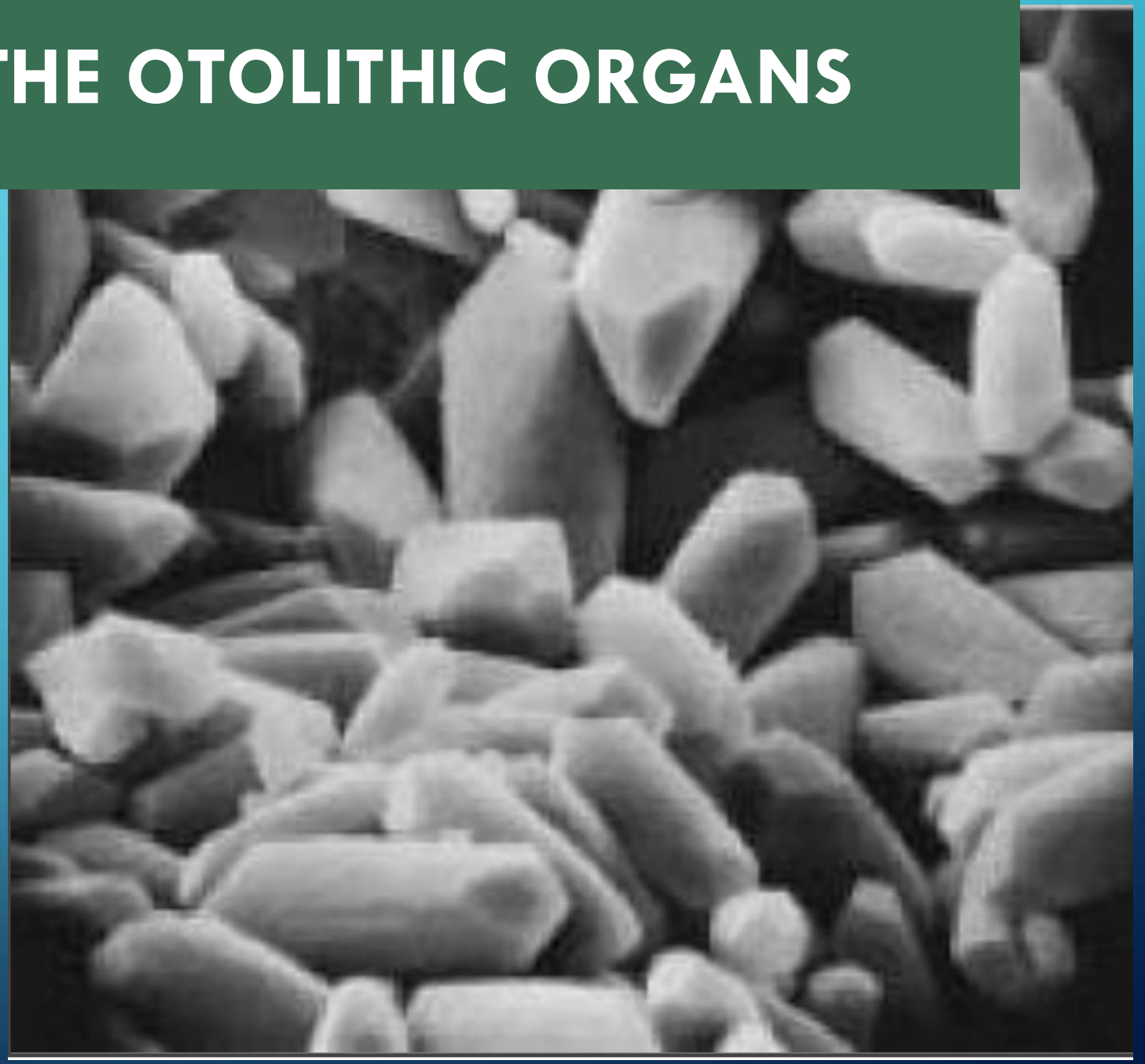
DEFINITION OF VERTIGO

First International Classification of Vestibular Disorders (ICVD-I) of the Barany Society

PHYSIOLOGY OF THE OTOLITHIC ORGANS

Otoliths:

- **Random size**
- **Random shape**
- **Random inertia**
- **Latency to full acceleration varies**



ISOLATED OTOLITH DYSFUNCTION

- Loss of otolith function disrupts that neural interaction and causes patient reports of disorientation as well as postural unsteadiness
- Many report dizziness, vertigo, and postural unsteadiness
- Tests in these patients may show all semicircular canals have normal function
- ***Dizzy patients with abnormal otolith function tests, despite a normal caloric response, are defined as having specific (isolated) otolith organ dysfunction.***

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6468282/

ISOLATED OTOLITH DYSFUNCTION (IOD)

- Tend to be older persons

- isolated otolith dysfunction (iOD) produces
  - Tilting
  - Translational sensations in the ***roll plane (***tilting, floating, rocking)
  - Translational sensations in the ***pitch plane*** or (tipping, floating, rocking)
  - Drop attacks or a falling sensation—have to grab on.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6468282/

ISOLATED OTOLITH DYSFUNCTION

Otolith function related symptoms

- Greater likelihood of swaying or rocking type dizziness than rotary vertigo
- Prodding gets the patient to realize the symptoms are different than spinning.
- Greater chance of abnormal
  - cVEMP and/or
  - oVEMP

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6468282/

ANOTHER NAME: OTOLITH ORGAN-SPECIFIC VESTIBULAR DYSFUNCTION (OSVD)

- **Must-have abnormalities:**
- cVEMP responses to air-conducted sound **and/or**
- oVEMP responses to bone-conducted vibration **and**
- normal caloric responses **and**
- normal video head impulse test (vHIT) recordings in each SCC plane.

ANOTHER NAME:
ISOLATED UTRICULAR DYSFUNCTION

Isolated utricular dysfunction (iUD)

- Defined as the presence of a unilateral oVEMP abnormality and normal caloric responses
- Could be isolated DVV in rotary chair testing?

Symptom plus lab: only otolith symptoms and normal calorics

Just lab based: normal calorics, only abnormal cVEMP and/or oVEMP

iOD of utricle (only oVEMP)	5 (45.5%)	1(8.3%)

Note that iOD of utricular origin was more common

iOD of utricle and saccule	3(27.3%)	1(8.3%)
iOD combined with other	**2(18.2%)**	**10(83.3%)**
iOD + BPPV	1(9.1%)	6(50%)

Again, note:

- This study excluded persons w a caloric deficit
- Intriguing: how many have isolated otolith dysfunction (iOD)

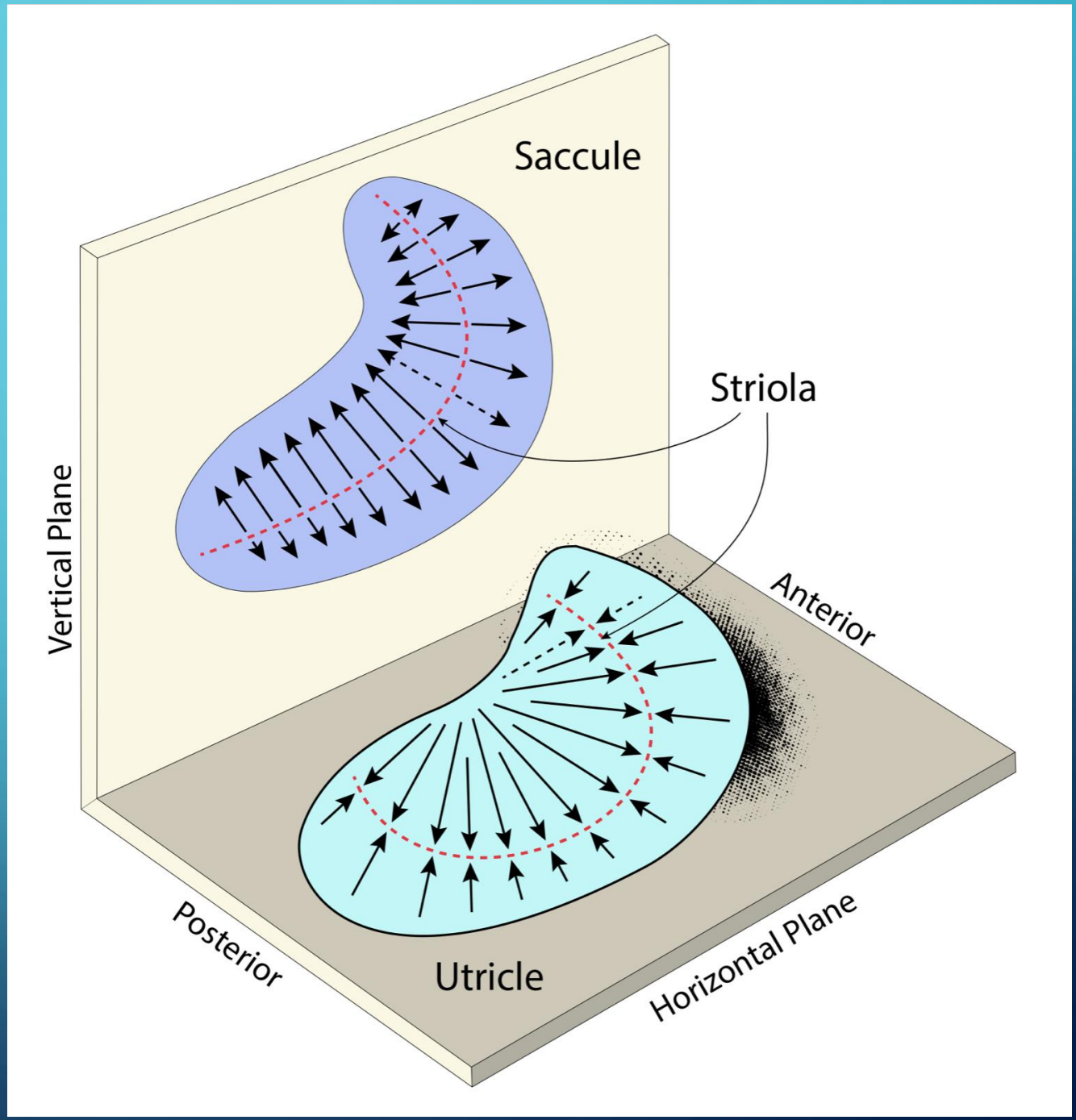
iOD+vestibular paroxysmia	0	1(8.3%)
Total	11	12

Otoltih organs
GravitoInertial Force (GIF) receptors

- Otolithic receptors are stimulated by gravitoinertial force (GIF)
- Gravity and Inertial force act (linear acceleration) on otoconia resulting in deflections of the hair bundles of otolithic receptor hair cells.
- The GIF is the sum of gravitational force and the inertial force due to linear acceleration.
- Integration of SCC and otolith input is required to tell the difference between static tilt and linear translation

STRIOLA: LINE OF POLARITY REVERSAL CALLED LPR

- Note the polarity of the hair cells
- Towards striola in the utricle
- Away from the striola in the saccule



GravitoInertial Force (GIF) receptors

- For a given linear acceleration, the opposite polarization of receptors across the striola
  - excites receptors on one side of the *line of polarity reversal* (LPR at the striola)
  - and simultaneously inhibits receptors on the opposite side of the LPR. (Leading to disfacilitation (hyperpolarization in response to stimulation across the striola)).

DO STIMULI ON OPPOSITE SIDES OF THE LPR CANCEL EACH OTHER?

- It would s… a should cancel.
- Instead of … ely polarized hair cells e…
- In *both* in…
- For the uti… nction

- **Note that linear acceleration is not symmetric on opposite sides of the head whereas rotational acceleration is symmetric.**
- **By comparison, then, the more activated macula has preference in CNS notice.**

Disfacilitation:
Dis – facilitation
A **form of inhibition during which neurons are hyperpolarized due to the temporal absence of excitatory synaptic activity**; i.e., hyperpolarization in the opposite otolith organ

INTEGRATION OF OTOLITH SYSTEMS

How are the two sustained and transient otolithic afferent systems complementary??

- **The sustained system** concerned with signaling
  - **low frequency GIF stimuli** such as (the ***sustained otolith system)***
    - Stimulated by head roll and head tilts
- **The transient system** which is activated
  - by sound and vibration and high acceleration tilt or linear translation.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5371610/

SUSTAINED VS TRANSIENT OTOLITH RECEPTORS

- Striolar specialized band of receptors along the striola
  - consist of mainly type I receptors
  - hair bundles are weakly tethered to the overlying otolithic

- 500-Hz vibration identifies the contribution of the transient system to vestibular controlled responses, such as vestibulo-ocular, vestibulo-spinal, and vestibulo-sympathetic responses.
- Intratympanic gentamicin preferentially attacks type I receptors.

signaling system of dynamic otolithic stimulation.

sound.

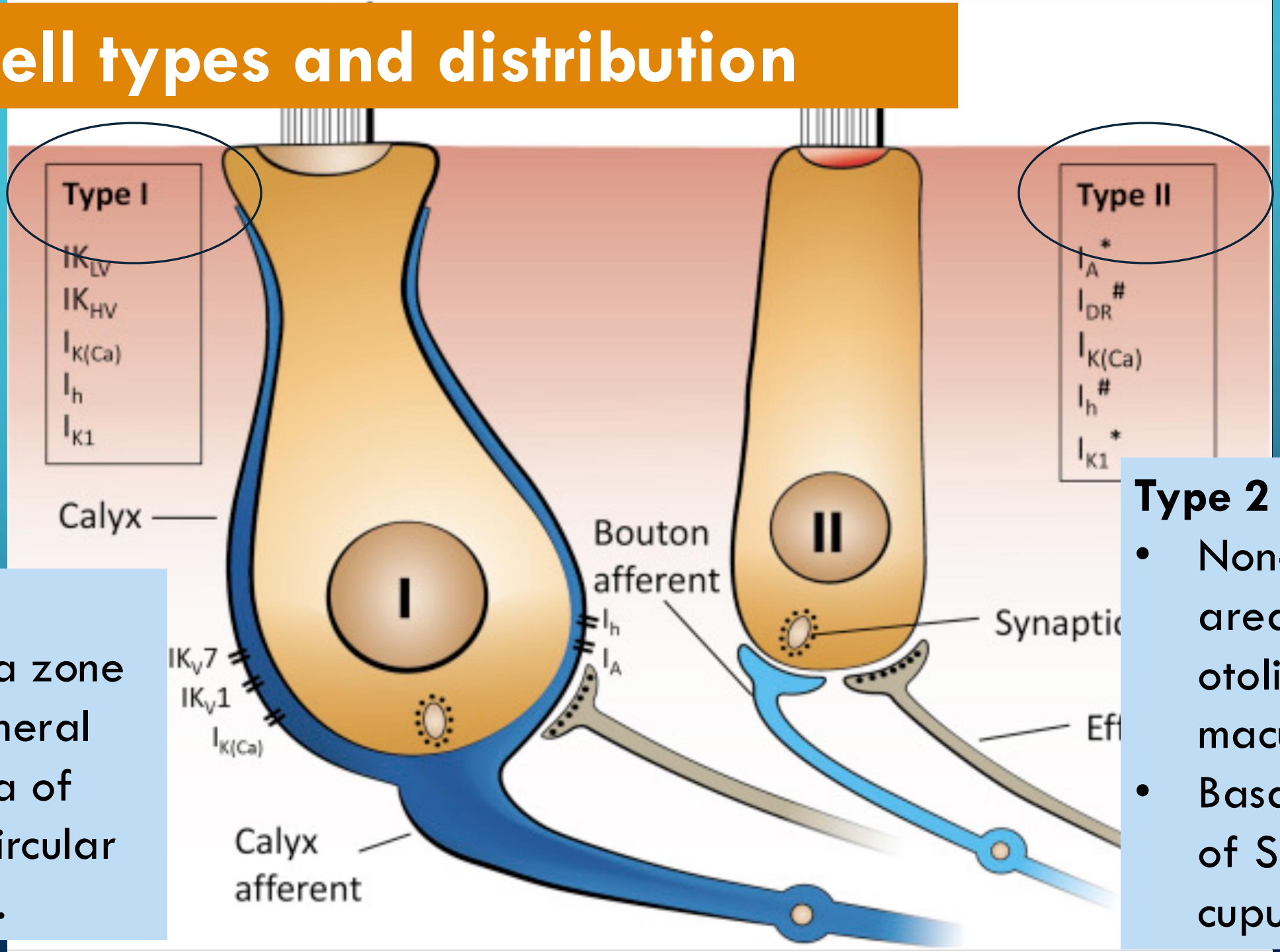
KEY CONCEPTS

- Vestibular afferents with ***regular resting discharge*** constitute a system for signaling sustained vestibular stimuli, such as maintained head tilts.

- These results show a similar pattern in all vestibular organs
  - primary semicircular canal and
  - otolithic neurons
- Useful to distinguish between responses to the
  - onset of an acceleration, as opposed
  - to responses during maintained accelerations

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5371610/

Hair cell types and distribution



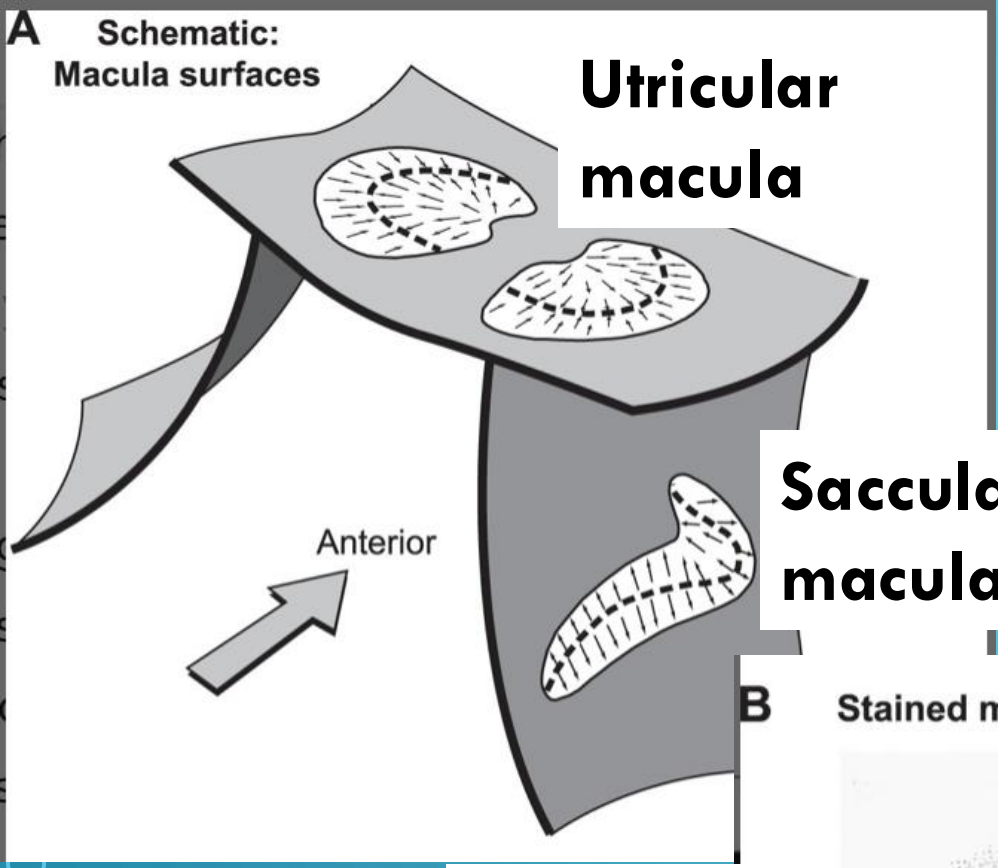
Type 1

- Striola zone
- Peripheral cupula of semicircular canal.

Type 2

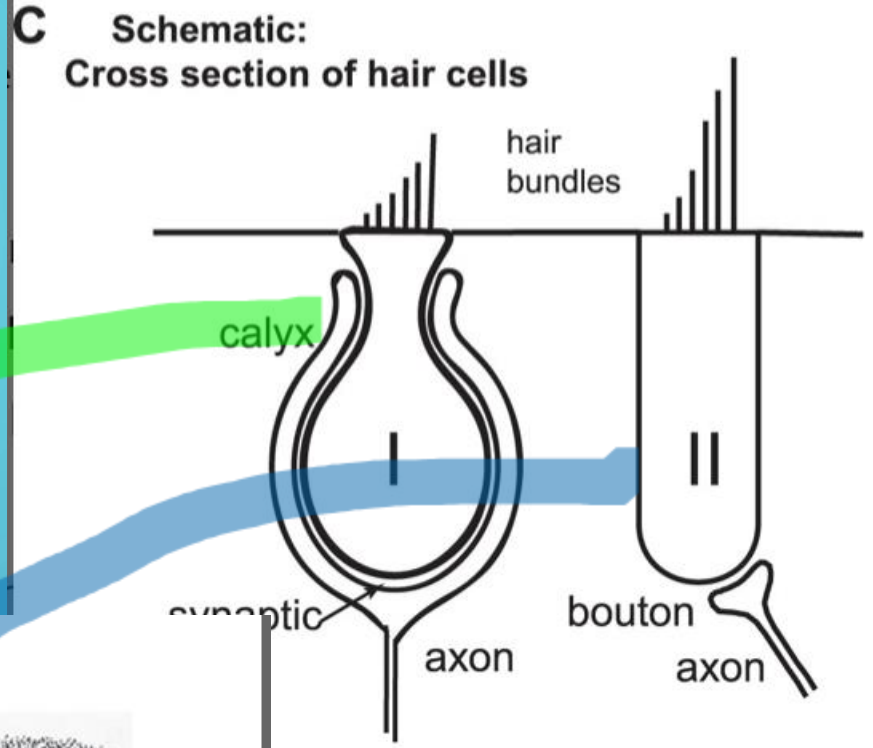
- Non-striolar areas of otolith macula
- Basal areas of SSC cupula

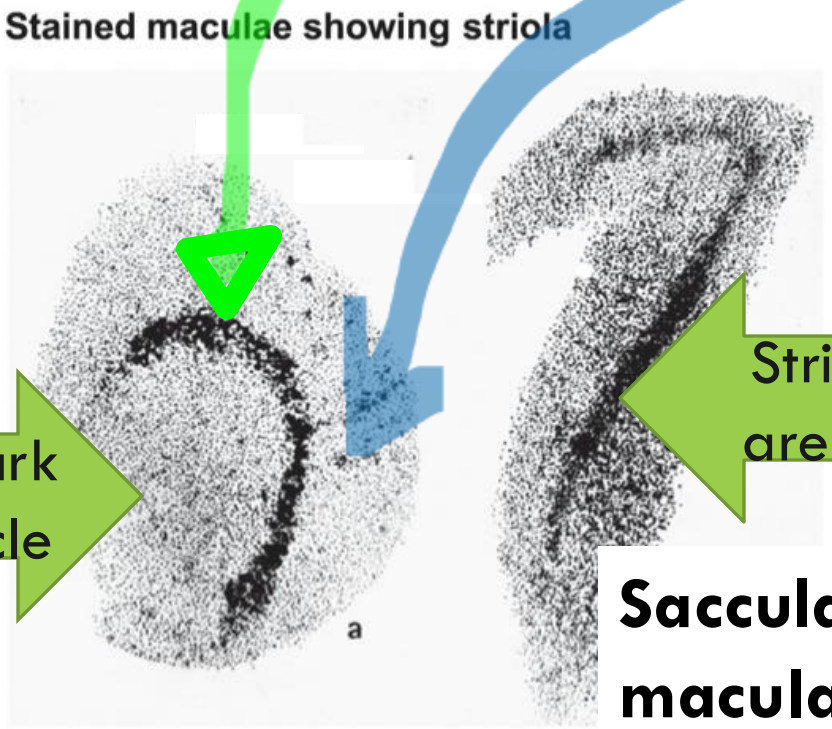
Guinea pig utricle and saccule



Utricular macula

Saccular macula





Utricular macula

Striola dark area utricle

Striola dark area saccule

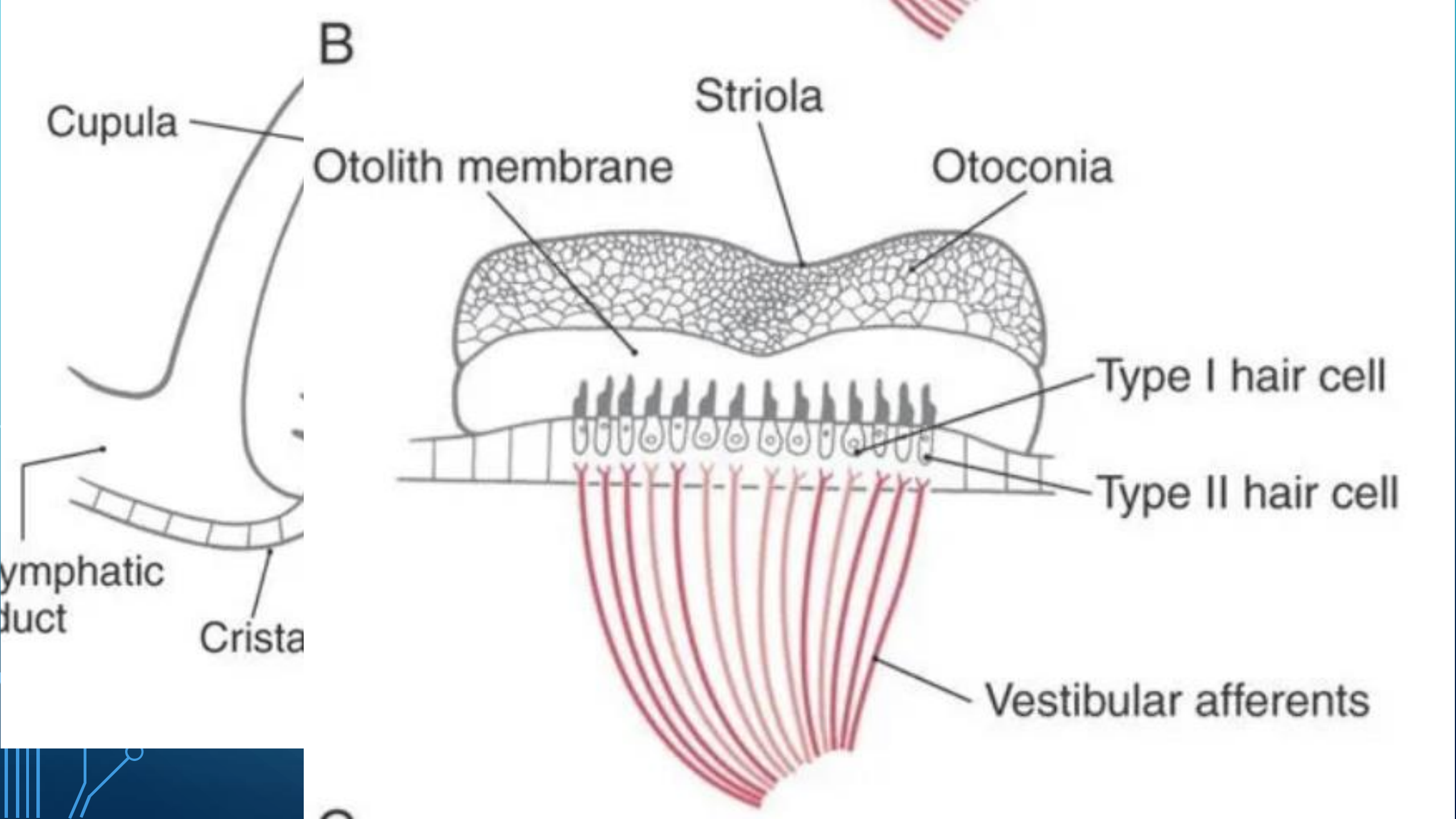
Saccular macula

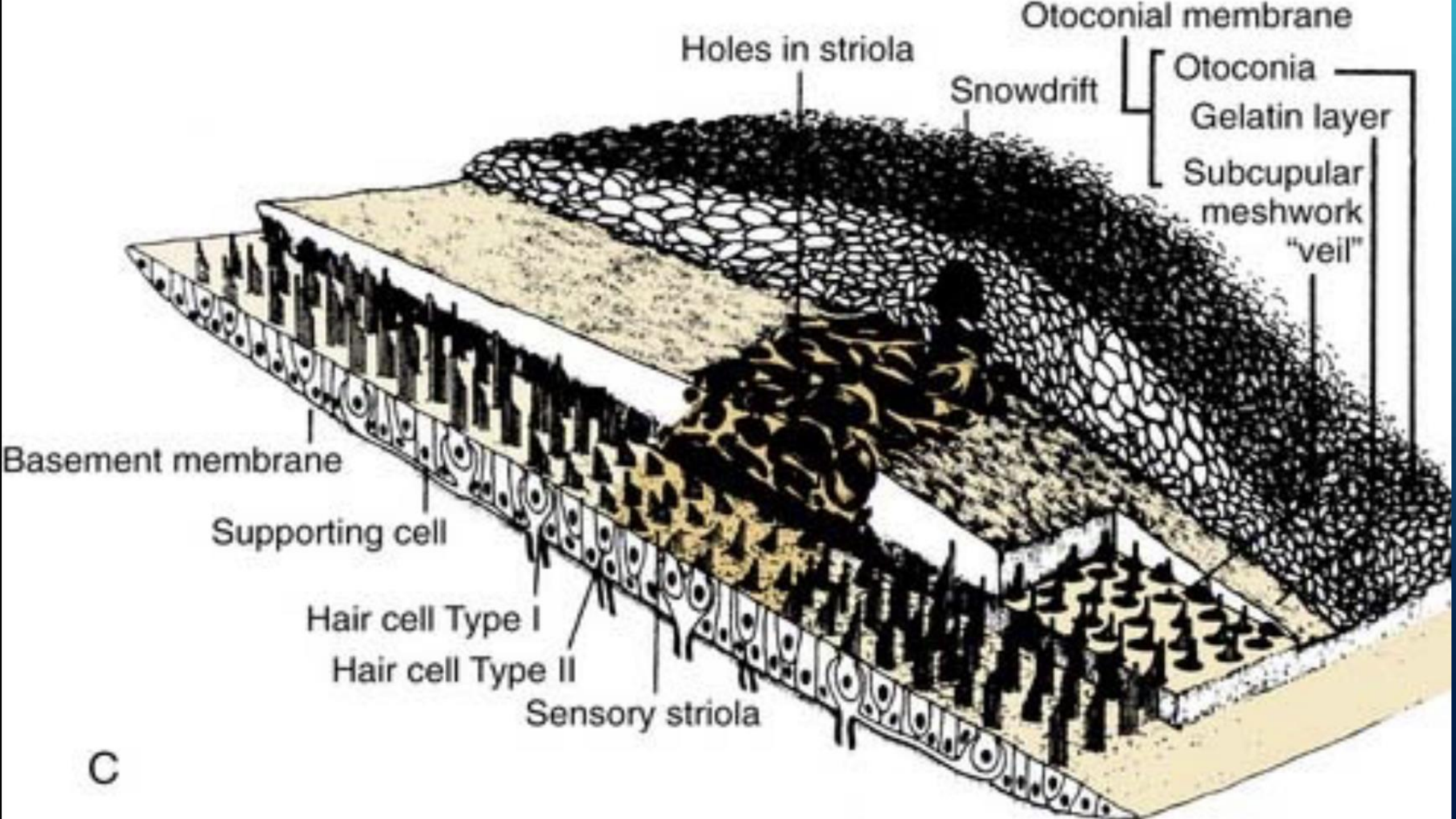
SEMICIRCULAR CANAL TYPE 1 VS TYPE 2 RECEPTORS

- In the canal system, transient type I receptors are at the ***crest of the crista,***
- The type II receptors are distributed ***throughout the crista.***

SLOW VS RAPID ONSET PERCEPTION

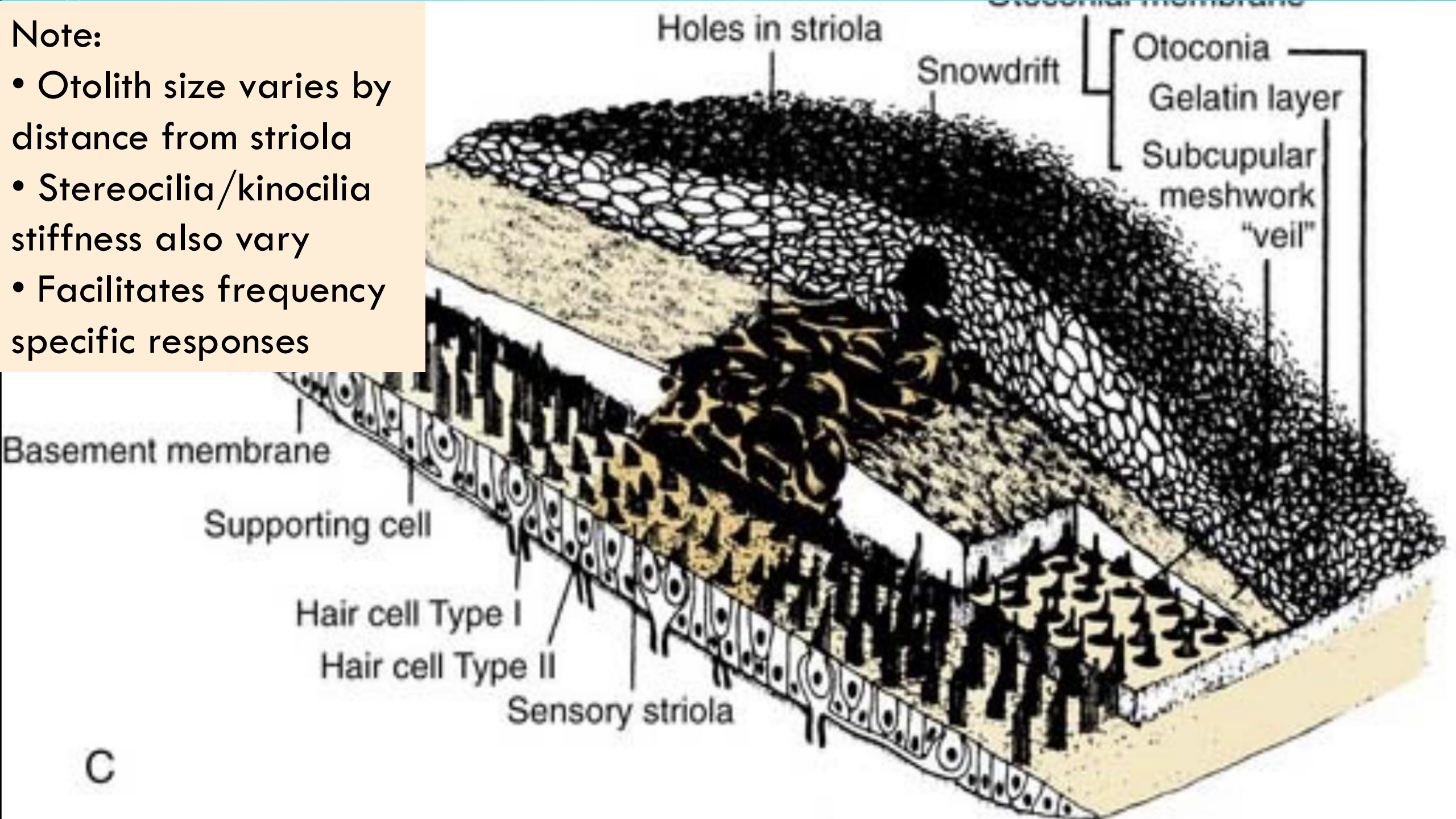
- The sustained canal system signals low-frequency, long-duration stimuli such as caloric stimuli.
- The transient canal system *probably* signals abrupt onset high-acceleration head impulse stimuli such as vHIT stimulation.
- I.e., the receptors are designed differently to look at slow and rapid acceleration features


Cupula
ymphatic
duct
Crista
B
Striola
Otolith membrane
Otoconia
Type I hair cell
Type II hair cell
Vestibular afferents

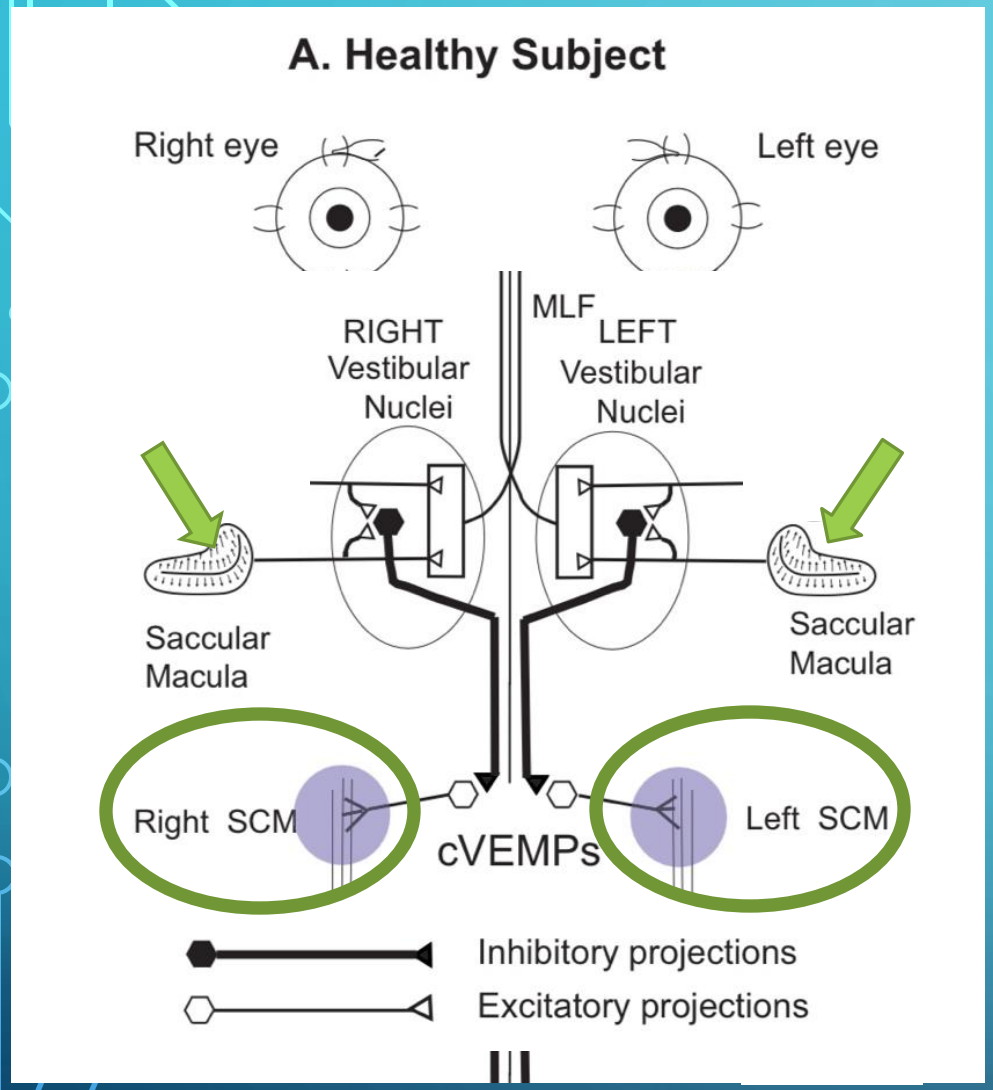

Otoconial membrane
Holes in striola
Otoconia
Snowdrift
Gelatin layer
Subcupular meshwork
"veil"
Basement membrane
Supporting cell
Hair cell Type I
Hair cell Type II
Sensory striola
C

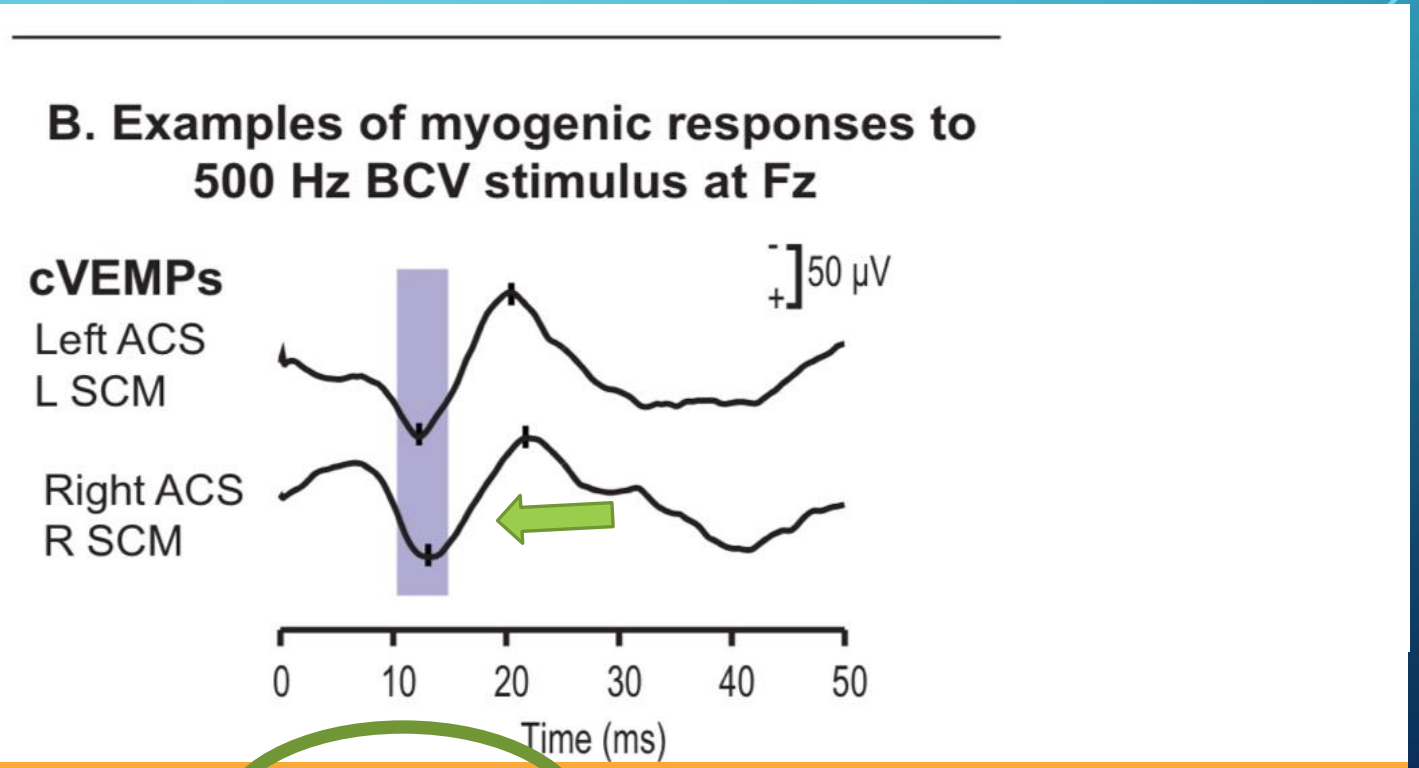
Note:

- Otolith size varies by distance from striola
- Stereocilia/kinocilia stiffness also vary
- Facilitates frequency specific responses



oVEMP Excitatory to inferior oblique muscle





cVEMP Inhibitory to ipsilateral SCM

DISFACILITATION

- A form of inhibition during which neurons are hyperpolarized due to the temporal absence of excitatory synaptic activity
- I.e., a process by which depolarization results in hyperpolarization of the less stimulated otolith organ

AGE RELATED DECLINE OF VESTIBULAR FUNCTION

- Significant declines in vestibular function with aging
  - In each of the semicircular canal planes
  - In utricular function
  - But not saccular function.
  - Symptom pattern then is global, all sensory surfaces

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3376350/

VESTIBULAR SENSORY LOSS IN DISEASE

- With vestibular neuritis, loss is patchy in the nerve
  - Likely also in the sensory apparatus
  - Symptoms depend on what sensory aspects are impaired
- With Meniere's,
  - Vestibular neuritis related loss
  - Hydrops related loss
- With trauma, loss depends on direction of maximum acceleration/deceleration
  - Less likely to be SSC
  - More likely to be otolith because acceleration is more linear

SYMPTOM PATTERNS TO LOOK FOR:

- With peripheral macular injury,
  - some assumed positions will be more symptomatic even while lying still
  - Rapid oscillating ocular counterroll blurry vision (also if vertical canals affected)
- With striolar injury, rapid movement will be more symptomatic, oscillopsia patterns of bouncing, side to side oscillation, fore/aft oscillation
- With whole-SSC canal cupular injury, rotation at slow and face pace will be affected, hHIT, horizontal head rotation oscillopsia
- With tip of SSC cupular injury, even over time, fast head movements will persist to be affected

ARE SYMPTOM PATTERNS BETTER THAN TESTING?

- VEMP is a whole striola response; may miss significant disease
- DVV is a whole non-striolar utricular macula response but the pattern may tell us somethings
  - Weak response
  - Perverse response
  - Not as sensitive as bent-forward sway testing
- Step testing: integration-adaptation vs symptom patterns; not very sensitive
- SHA: CNS adaptation vs symptoms, moderately sensitive
- Calorics: very slow, not fast movement correlated
- Positional nystagmus: nonadapted, CNS vs peripheral

TIME TO PAUSE FOR ANOTHER DAY

QUESTIONS?

VEMP AND STOCHASTIC SIGNALS.

- VEMP can be induced not only by transient sounds but also by a continuous stimulation with a stochastic signal.

STOCHASTIC

- The word *stochastic* in English was originally used as an adjective with the definition "pertaining to conjecturing", and stemming from a Greek word meaning "to aim at a mark, guess", and the Oxford English Dictionary gives the year 1662 as its earliest occurrence. It has been translated to mean "the art of conjecturing or stochastics." This phrase is used with a sense meaning random.

STOCHASTIC RESONANCE

- **Stochastic resonance is a phenomenon that occurs in a threshold measurement system when an appropriate measure of information transfer is maximized in the presence of a non-zero level of stochastic (high level random) input noise thereby lowering the response threshold;[1] the system resonates at a particular noise level.**
- **The implication is input that does not allow neural cellular repolarization.**
- **Depolarization then is random and VEMP responses can then be tuned across frequencies**
- **Tunable responses may provide information on physiologic changes in kinociliary/stereociliary stiffness in health and in disease**