READING: 5.2; 14.1; Hemispherectomy story on website

Learning from rarities/oddities in nature

Main Points

1. Even injury is dynamic process

2. Intervention possible at many levels

3. Balance between specialization/differentiation and plasticity

Study questions

1. What factors influence the behavioral/cognitive outcome of a neurological injury? Give as many different kinds of answers as possible.

Why might studying arctic ground squirrels help treatment of brain trauma?

Your friend in his 20's is at a party and is having trouble getting words out and the right side of his body is numb and weak. What should you do?

A. Ask if he wants help and do what he wants

B. Take away his keys and put him to bed

C. Post embarrassing videos of him on facebook

D. Wait a few hours and if symptoms persist, take him to the doctor

E. Get to the emergency room immediately

The person described in the last question has very likely suffered from

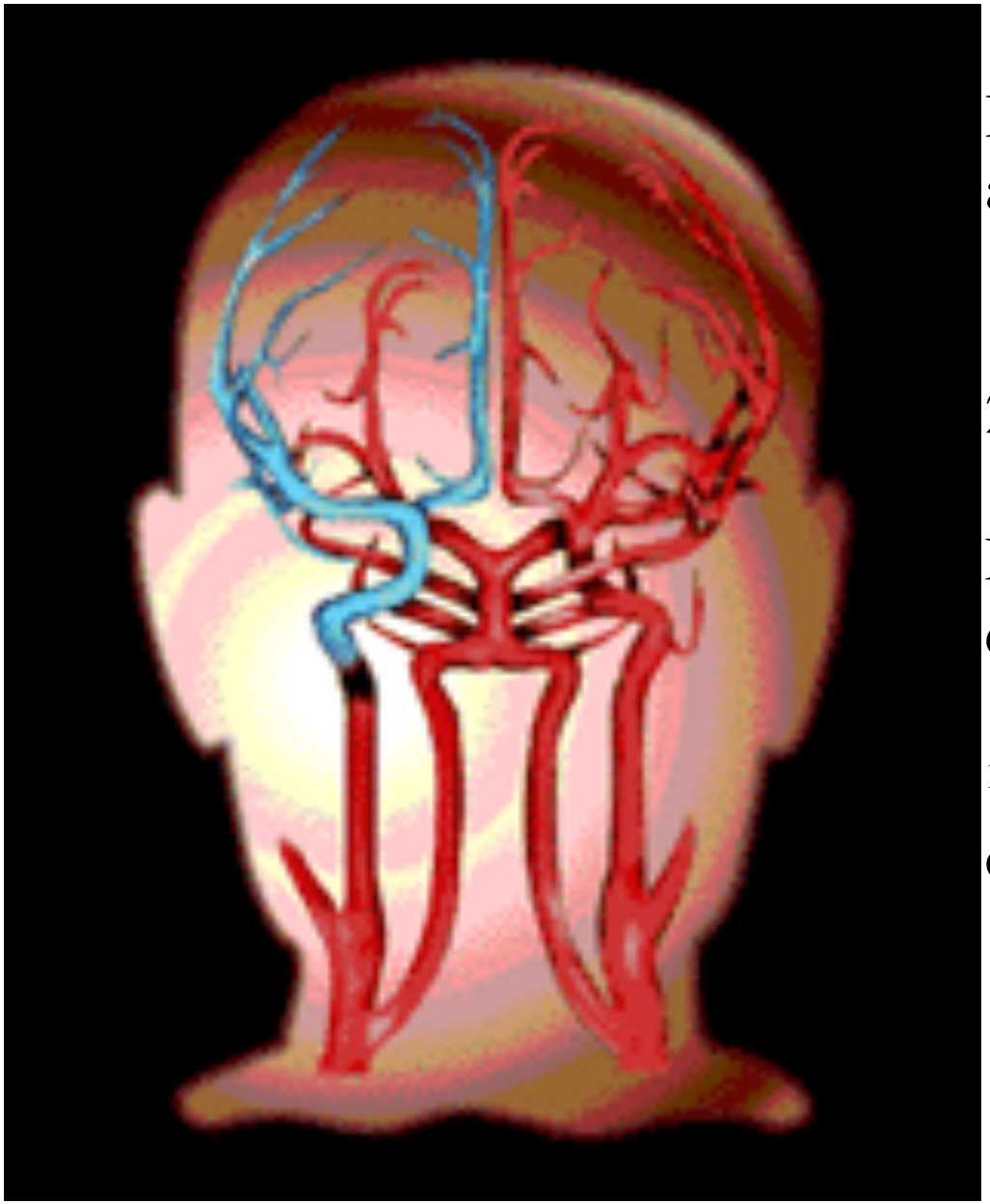
A. Stroke

B. Epilepsy

C. Drunkenness

D. Heart attack

E. Narcolepsy



Kinds of brain injury in adulthood

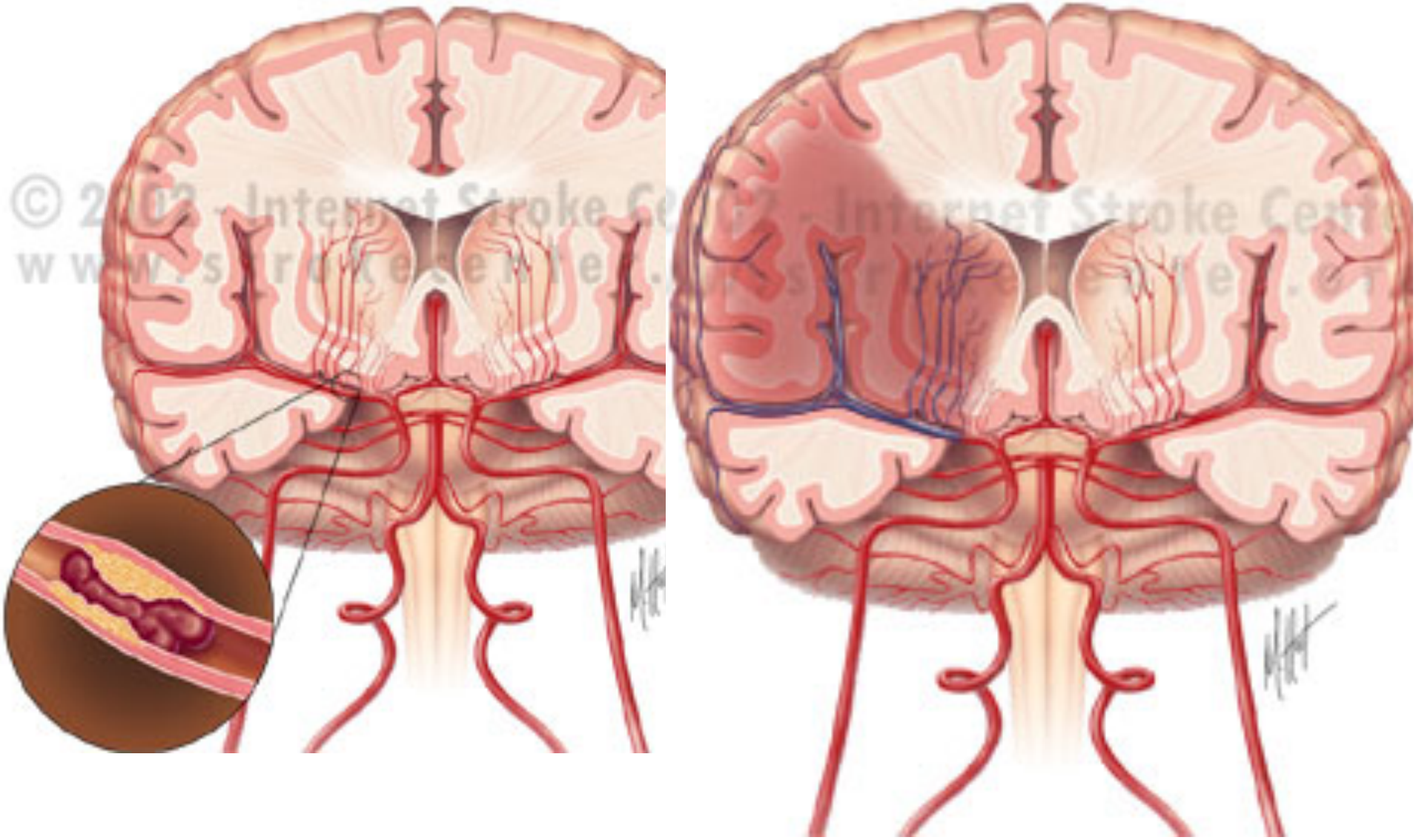
Stroke -- loss of blood supply

2nd leading cause of death

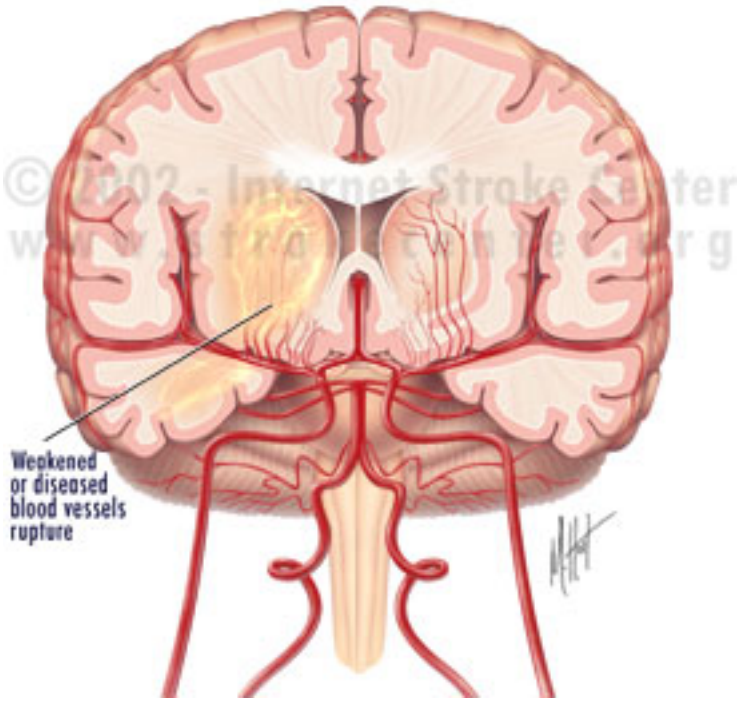
Leading cause of adult disability

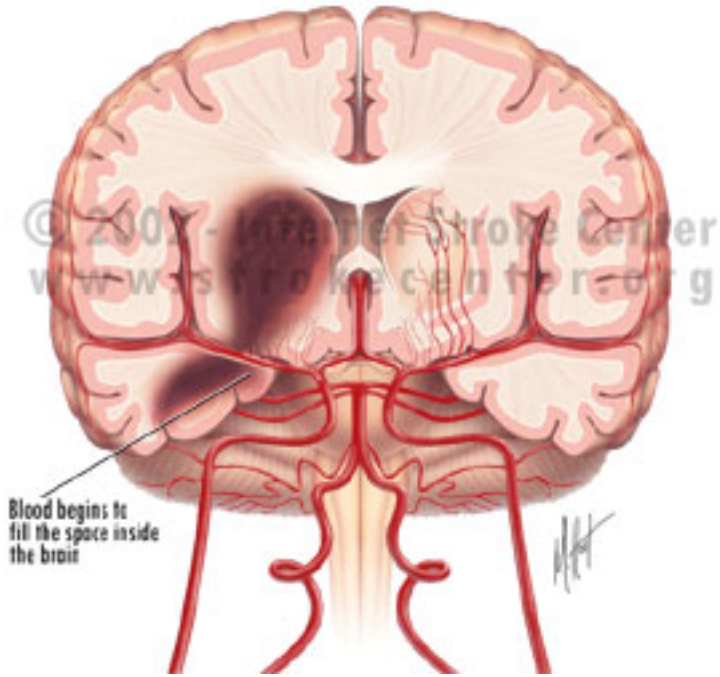
½ of survivors dependent on others for daily living

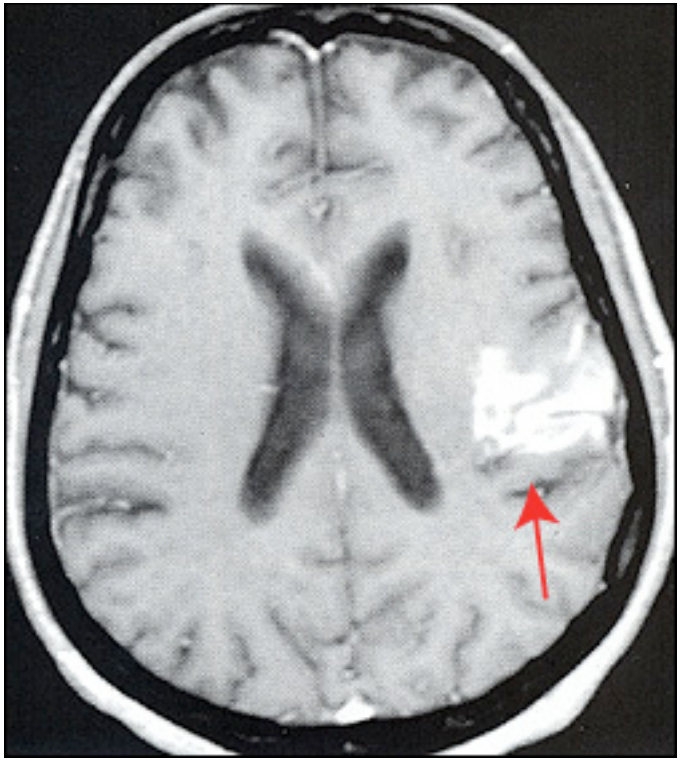
Ischemic - clots



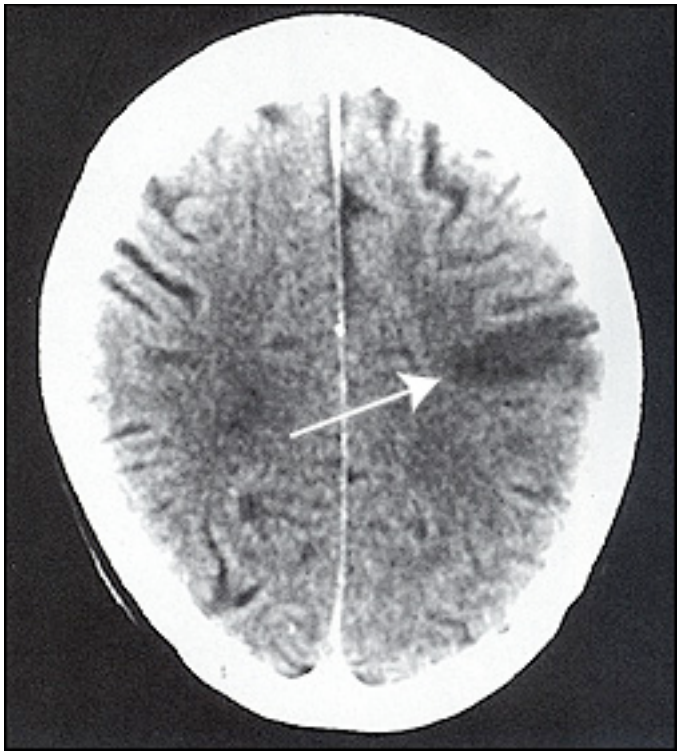
Hemorrhagic – bleeding







MRI of a patient who has had a stroke of the left hemisphere of the brain. The arrow indicates the area that was affected.



CT scan of a patient who has had a left middle cerebral artery stroke. The arrow indicates the location of the stroke

NIHSS Results

1a - Level of Consciousness	
1b - LOC Questions	
1c - LOC Commands	
2 - Best Gaze	
3 - Visual Fields	
4 - Facial Palsy	
5a - Left arm	
5b - Right arm	3
6a - Left leg	
6b - Right leg	
7 - Limb ataxia	
8 - Sensory	
9 - Best Language	2
10 - Dysarthria	2
11 - Extinction	

Close

NIHSS Score: 7

Research

Association of laterality and size of perfusion lesions on neurological deficit in acute supratentorial stroke

Meng Lee[1,5], Jeffrey L. Saver[1], Jeffry R. Alger[1], Qing Hao[1], Noriko Salamon[2], Sidney Starkman[1,3], Latisha K. Ali[1], Bruce Ovbiagele[1], Doojin Kim[1], J Pablo Villablanca[2], Michael T. Froehler[1], Matthew S. Tenser[4], David S. Liebeskind[1,*]

Article first published online: 8 DEC 2011

DOI: 10.1111/j.1747-4949.2011.00726.x

Issue

International Journal of Stroke

Volume 7, Issue 4, pages 293–297, June 2012

Table 1. Characteristics of first-ever right-handed left and right-hemisphere stroke patients

Characteristics	Left-hemisphere stroke, *n* = 58	Right-hemisphere stroke, *n* = 53
Age, year	64·5 (interquartile range 50–79)	65 (interquartile range 59–78)
Male, *n* (%)	30 (52%)	19 (36%)
NIHSS score	10 (interquartile range 4–19)	8 (interquartile range 3–14)
Ischaemic volume (ml)	53 (interquartile range 26–92)	65 (interquartile range 32–120)
Time interval between LNW to PWI (minutes)	350 (interquartile range 250–520)	390 (interquartile range 260–540)

Category	Score/Description		Date/Time Initials	Date/Time Initials	Date/Time Initials	Date/Time Initials	Date/Time Initials
1a. **Level of Consciousness** (Alert, drowsy, etc.)	0 = Alert 1 = Drowsy 2 = Stuporous 3 = Coma						
1b. **LOC Questions** (Month, age)	0 = Answers both correctly 1 = Answers one correctly 2 = Incorrect						
1c. **LOC Commands** (Open/close eyes, make fist/let go)	0 = Obeys both correctly 1 = Obeys one correctly 2 = Incorrect						
2. **Best Gaze** (Eyes open - patient follows examiner's finger or face)	0 = Normal 1 = Partial gaze palsy 2 = Forced deviation						
3. **Visual Fields** (Introduce visual stimulus/threat to pt's visual field quadrants)	0 = No visual loss 1 = Partial Hemianopia 2 = Complete Hemianopia 3 = Bilateral Hemianopia (Blind)						
4. **Facial Paresis** (Show teeth, raise eyebrows and squeeze eyes shut)	0 = Normal 1 = Minor 2 = Partial 3 = Complete						
5a. **Motor Arm - Left** 5b. **Motor Arm - Right** (Elevate arm to 90° if patient is sitting, 45° if supine)	0 = No drift 1 = Drift 2 = Can't resist gravity 3 = No effort against gravity 4 = No movement X = Untestable (Joint fusion or limb amp)	Left					
		Right					
6a. **Motor Leg - Left**	0 = No drift 1 = Drift	Left					

Table 3. Relationship between ischaemic vegression analyses

	Median scores of NIHSS (left, right)	Increase of odds of NIHSS scoring if stroke at left brain
1a. Level of consciousness	0, 0	1·36 (P = 0·605)
1b. LOC Questions	1, 0	25·53 (P < 0·001)
1c. LOC Commands	0, 0	80·40 (P = 0·01)
2. Gaze	0, 0	1·15 (P = 0·775)
3. Visual	0, 0	1·48 (P = 0·395)
4. Facial palsy	2, 1	1·72 (P = 0·176)
5a. Motor arm, left	0, 2	0·001 (P < 0·001)
5b. Motor arm, right	2, 0	222·07 (P < 0·001)
6a. Motor leg, left	0, 1	0·05 (P < 0·001)
6b. Motor leg, right	1, 0	97·13 (P < 0·001)
7. Limb ataxia	0, 0	1·22 (P = 0·841)
8. Sensory	0, 1	0·84 (P = 0·668)
9. Language	2, 0	306·43 (P < 0·001)
10. Dysarthria	1, 1	1·30 (P = 0·513)
11. Extinction/inattention	0, 1	0·11 (P < 0·001)
Total	10, 8	2·98 (P = 0·004)

NIHSS, National Institutes of Health

Lateralization

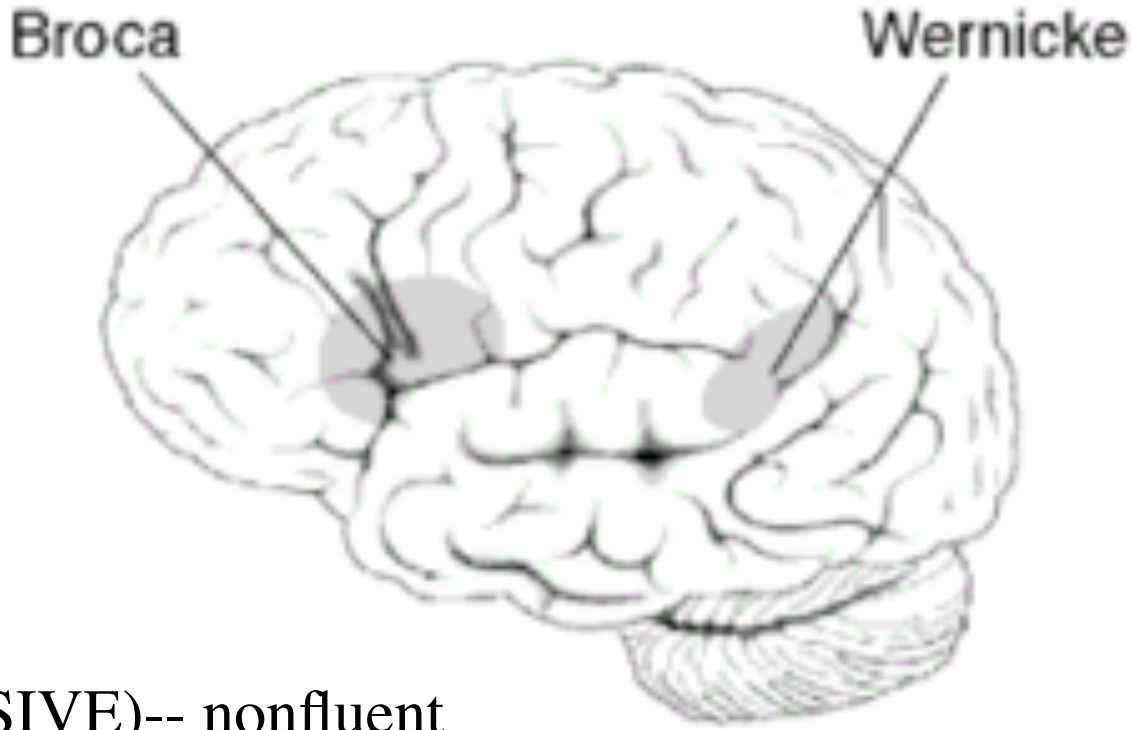
- Language -left hemisphere
- Wada test
- LH versus RH stroke
- 95% of aphasia (language impairment) due to LH damage

Localization of function

- specific parts of the brain perform specific functions
- structure x does y

Equipotentiality

- all parts of brain are equally competent to do y



Broca's aphasia (EXPRESSIVE)-- nonfluent aphasia, difficulty in word production/ grammar

Wernicke's aphasia (RECEPTIVE) -- fluent aphasia, word salad (anomia), poor comprehension

Broca's aphasia with
severe agrammatism

Broca’s Aphasia

slow and halting speech

struggle to get certain words out, such as the names of objects, places or people

speech content stripped down to simple elements

only contains basic nouns and verbs ("want drink”)

writing ability is often similarly affected

may be able to understand some spoken language, but have difficulty understanding grammar. They may be unable to tell the difference between, "Maureen slapped the naughty boy" and "the naughty boy slapped Maureen."

ht

Wernicke's aphasia: Answering interview questions

ht

Wernicke’s Aphasia

speak fluently using long sentences,

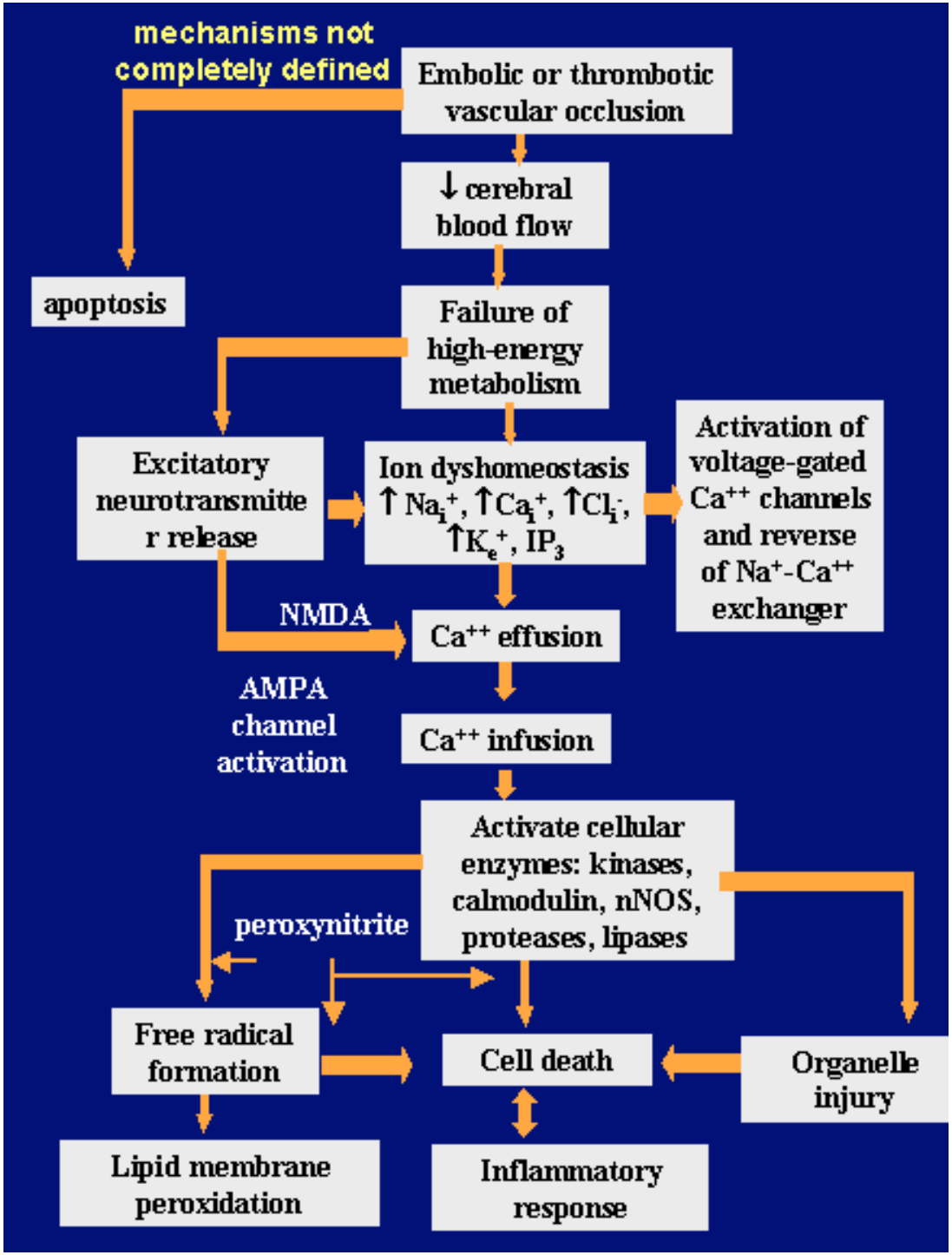
speech lacks meaning and often includes nonsense words.

Same difficulty may also occur when they write.

They may have difficulty understanding what people say, and what written words mean.

They often don't realise that they have difficulty understanding, and don't know why people can't understand them.

Neural processes after stroke



Mechanisms of injury

Cells die from lack of glucose/oxygen
- "Penumbra" exposed to waste products
- Fluid accumulates (edema)
- Glia dump glutamate
- Over-excitation kills additional cells
- Possible that cells turn on death genes (apoptosis)

Further afield (other problems)
- Distant areas (connected to stroke area) depress activity = diaschisis
  - Need to engage these areas in days after stroke

Mechanisms of recovery

1. Little by way of replacing cells

2. Engage untapped power of existing mechanisms

E.g., de-afferentation of limb causes loss of use of that limb. Not because lose control. If force use, animals/humans develop skills with them.

3. Regrow axons

periphery - good with myelin tract

In CNS – glia inhibit

Mechanisms of recovery

4. Resprouting -- NORMAL PROCESS
   neurotrophins → collateral sprouting
   lesion momentum

5. Denervation (or disuse) supersensitivity

6. Reorganize/rewire tissues

Mechanisms of recovery

Treatments

- tPA – tissue plasminogen activator
  - dissolves clots (3 h window only)
- hypothermia – prevents cell death in animals?
- antagonize glutamate – careful!!!!
- occupational therapy

Brain cooling after cardiac arrest

w cooling	35% minimal disability	50% mortality
without cooling	21%	67%

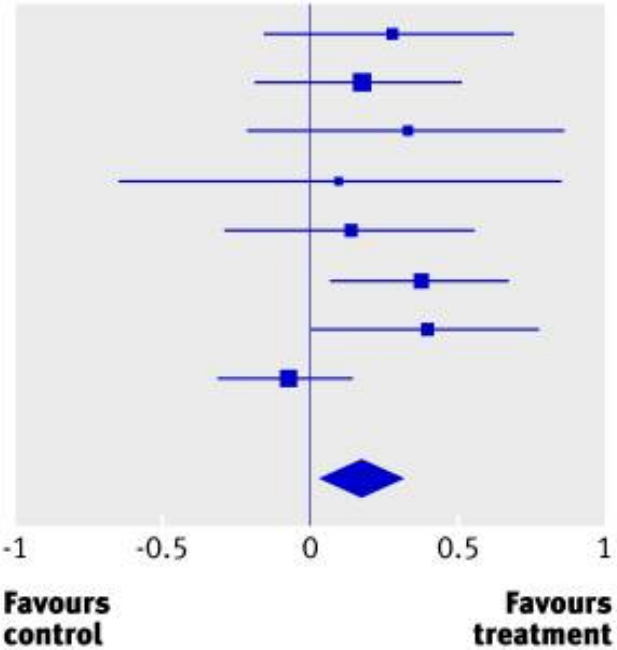
Doesn't work in conscious patients

Meta-analysis – looking at multiple studies together
Does occupational therapy help?? YES for daily activities

Study	Treatment No	Treatment Mean (SD)	Control No	Control Mean (SD)	Standard mean difference (random) (95% CI)
Corr 1995[w17]	46	12.30 (4.74)	39	10.87 (5.72)	0.27 (-0.16 to 0.70)
Gilbertson 2000[w18]	60	16.17 (3.76)	62	15.45 (4.48)	0.17 (-0.18 to 0.53)
Chiu 2004[w19]	30	108.90 (11.60)	23	104.90 (12.00)	0.33 (-0.21 to 0.88)
Walker 1996[w21]	12	10.75 (3.86)	15	10.33 (4.19)	0.10 (-0.66 to 0.86)
Logan 1997[w22]	45	15.42 (4.64)	38	14.82 (3.97)	0.14 (-0.30 to 0.57)
Walker 1999[w23]	84	18.44 (2.72)	79	17.35 (3.05)	0.38 (0.07 to 0.69)
Sackley 2006[w24]	53	10.21 (5.90)	47	8.09 (4.45)	0.40 (0.00 to 0.80)
Parker 2001[w25]	218	15.77 (4.04)	110	16.08 (3.87)	-0.08 (-0.31 to 0.15)
Total (95% CI)	548		413		0.18 (0.04 to 0.32)

Test for heterogeneity: χ^2=8.08, df=7, P=0.33, I^2=13.3%

Test for overall effect: z=2.45, P=0.01



The effect is about 1 point on this scale of daily activities – not huge

The Barthel Index

Bowels
0 = incontinent (or needs to be given enemata)
1 = occasional accident (once/week)
2 = continent
Patient's Score: _____

Bladder
0 = incontinent, or catheterized and unable to manage
1 = occasional accident (max. once per 24 hours)
2 = continent (for over 7 days)
Patient's Score: _____

Grooming
0 = needs help with personal care
1 = independent face/hair/teeth/shaving (implements provided)
Patient's Score: _____

Toilet use
0 = dependent
1 = needs some help, but can do something alone
2 = independent (on and off, dressing, wiping)
Patient's Score: _____

Feeding
0 = unable
1 = needs help cutting, spreading butter, etc.
2 = independent (food provided within reach)
Patient's Score: _____

Transfer
0 = unable – no sitting balance
1 = major help (one or two people, physical), can sit
2 = minor help (verbal or physical)
3 = independent
Patient's Score: _____

Mobility
0 = immobile
1 = wheelchair independent, including corners, etc.
2 = walks with help of one person (verbal or physical)
3 = independent (but may use any aid, e.g., stick)
Patient's Score: _____

Dressing
0 = dependent
1 = needs help, but can do about half unaided
2 = independent (including buttons, zips, laces, etc.)
Patient's Score: _____

Stairs
0 = unable
1 = needs help (verbal, physical, carrying aid)
2 = independent up and down
Patient's Score: _____

Bathing
0 = dependent
1 = independent (or in shower)
Patient's Score: _____

Total Score: _____

(Collin et al., 1988)

For 100 people treated, 11 avoided “poor” outcome

Reducing excessive GABA-mediated tonic inhibition promotes functional recovery after stroke

Andrew N. Clarkson, Ben S. Huang, Sarah E. MacIsaac, Istvan Mody & S. Thomas Carmichael

Affiliations | Contributions | Corresponding author

Nature **468**, 305–309 (11 November 2010) | doi:10.1038/nature09511

Received 30 November 2009 | Accepted 16 September 2010 | Published online 03 November 2010

Animal model of stroke

induce a stroke on one side to get motor symptoms

various walking tasks – on a grid, etc

measure paw use, foot fall errors etc

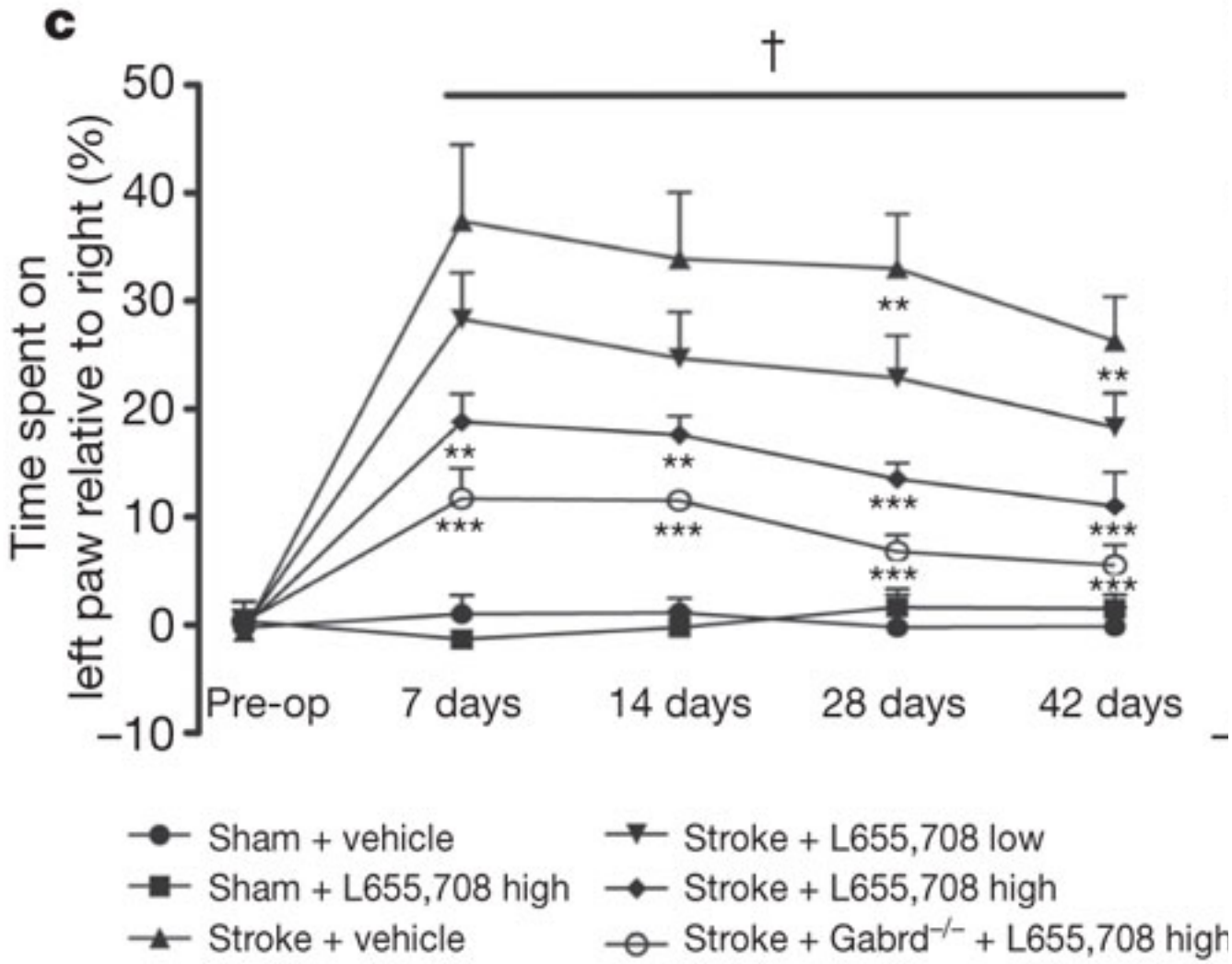
Drug L655, 708

antagonizes GABA-$_A$ receptor

Start 3 days after stroke

Sham = surgery but no stroke

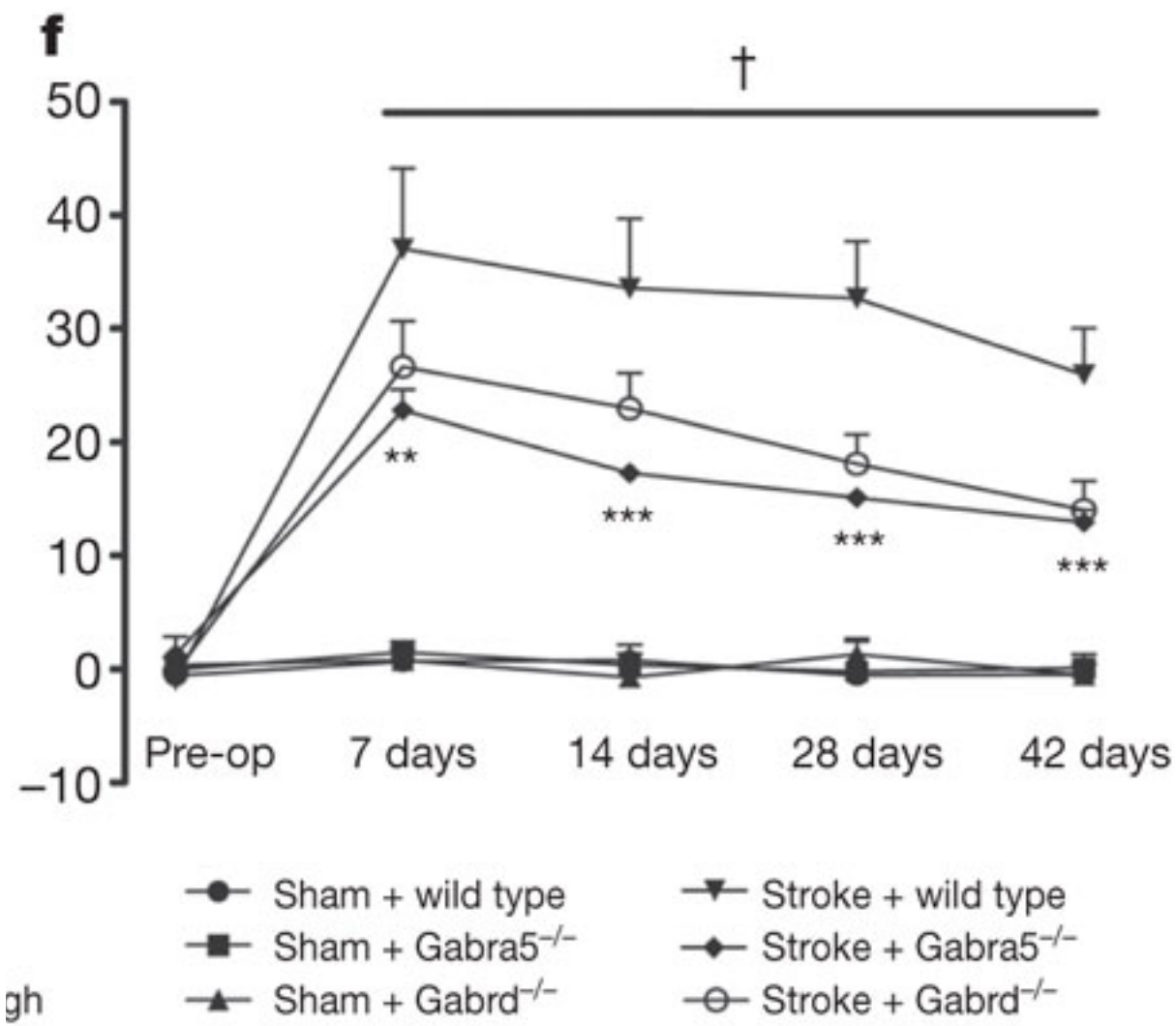
Vehicle = Injection but no drug



Genetic manipulations

Gabra5-/- lacks α5-subunit of $GABA_A$ receptor

Gabrd-/- lacks δ-subunit of $GABA_A$ receptors



wild type = genetically normal mice

Self-test question

What statement best characterizes the effective use of GABA antagonists after stroke

A. They help prevent immediately loss of cells

B. They prevent cell death from excito-toxicity

C. They counter inhibition after stroke

D. They just produce a more active brain which is useful in any context

E. All of the above

Self-test question

Which stroke would most likely cause a person to produce rambling sentences that don't make any sense

A. Left frontal

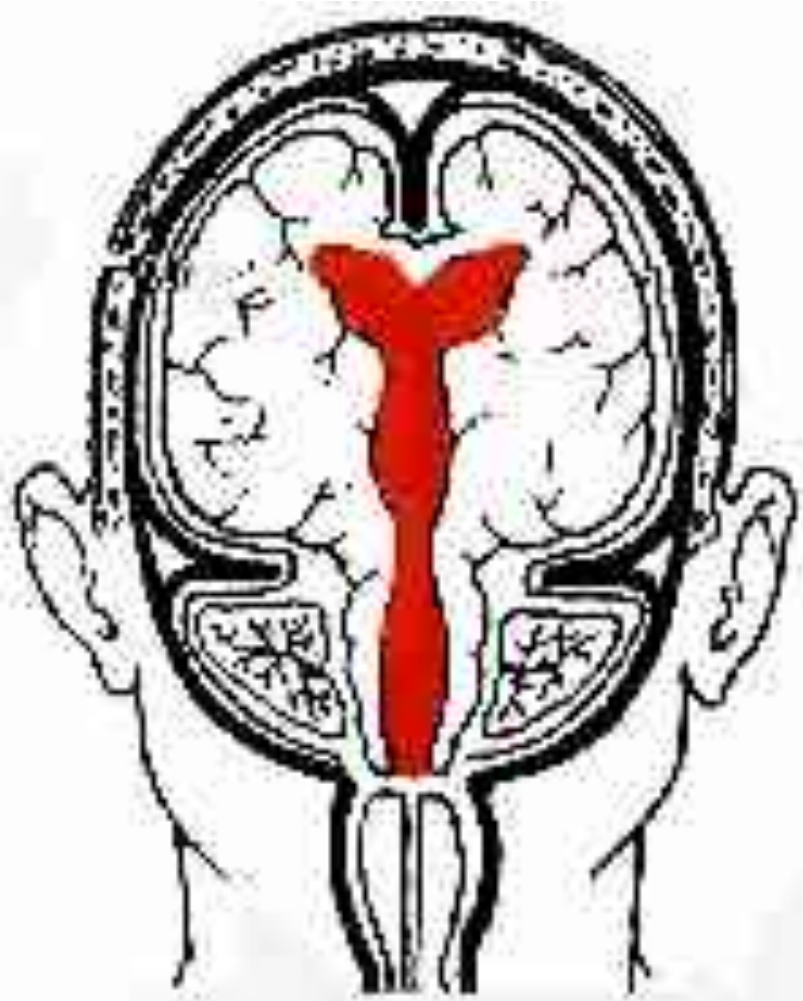
B. Left temporal

C. Right occipital

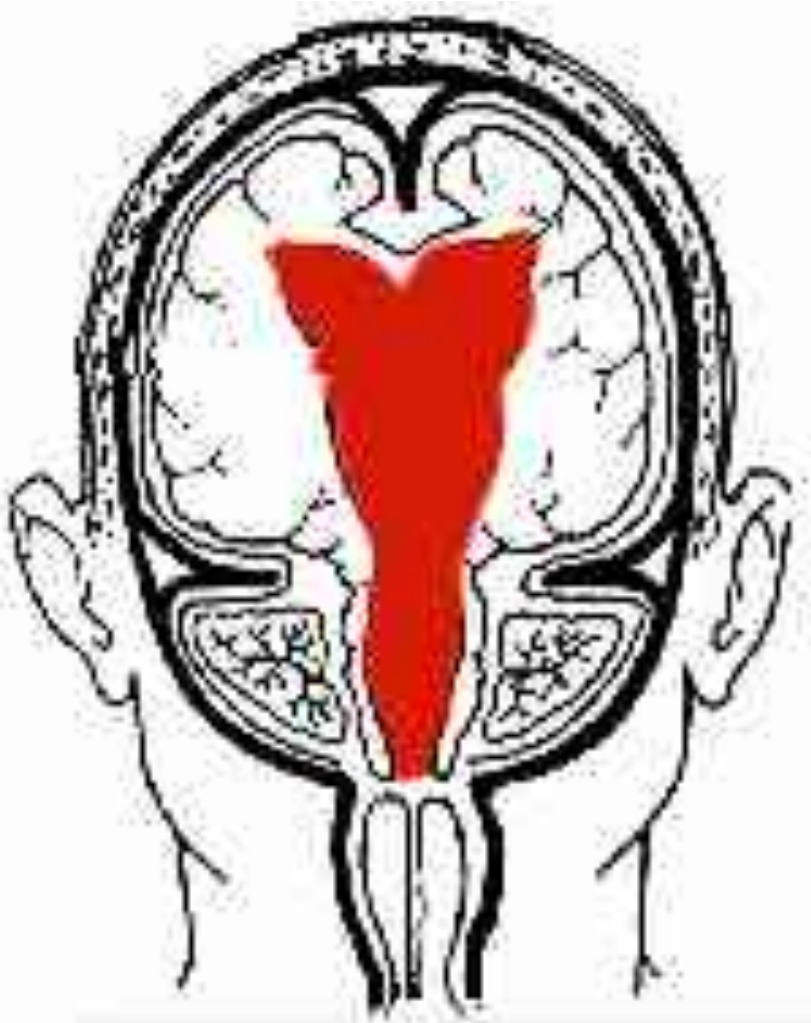
D. Right frontal

E. All are equally likely

Hydrocephalus



Normal ventricles



Enlarged ventricles

Modified from Iwoa Virtual Hospital


R
512*

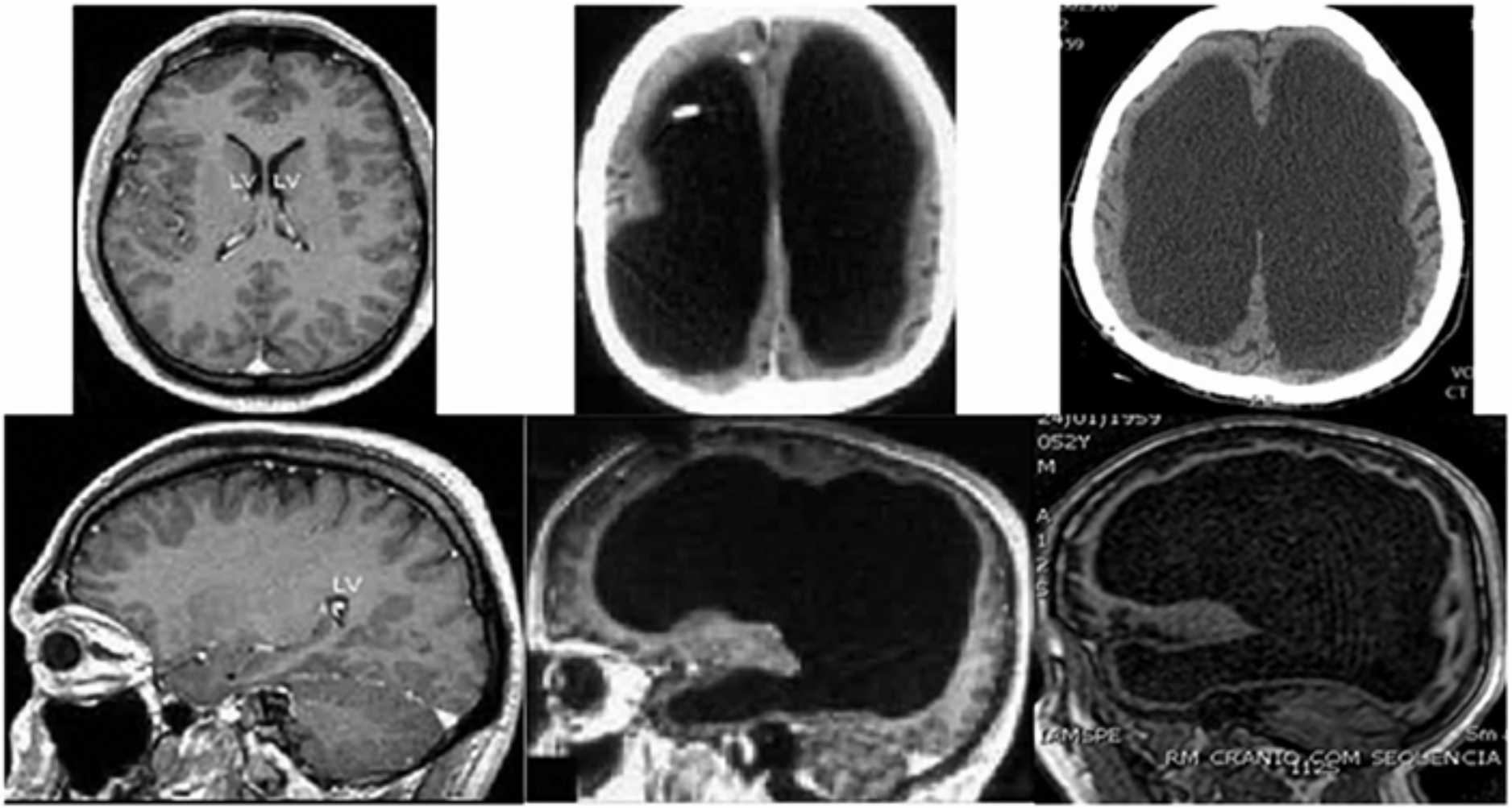
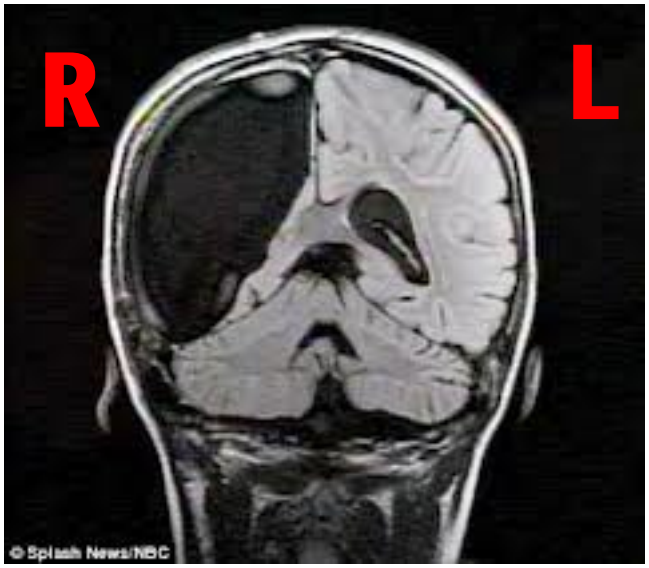


Figure 1. The contrast among a normal brain in a normal adult (left), the brain of a normal man with impressive hydrocephalus (Oliveira et al., unpublished data; middle), and an equally impressive hydrocephalus in a 54-year-old man with deep cognitive and motor impairment since childhood (right; Oliveira et al., unpublished data).

Cameron Mott video

Rasmussen's Syndrome
http://www.youtube.com/watch?v=2MKNsI5CWoU



Rasmussen's syndrome

epilepsy takes over one hemisphere of the brain

starts in childhood

remove the dysfunctional hemisphere

even removal of the left hemisphere allows language

in the remaining hemisphere

???because the damage is progressive

the OK hemisphere is training itself

removal removes interference of the dysfunctional hemisphere

extraordinary abilities to recover function

Kid develops left hemisphere epilepsy at 5 y 6 m

fMRI at 6 y 10 mo: left hemisphere language dominance

Remove left hemisphere at 9 y: profound aphasia and alexia

Starts getting comprehension back quickly

fMRI at 10 y 6 mo: right hemisphere activation with language tasks

What about adults?

Rarely done – thought to have lost some plasticity

53 year old, suffered head injury at 5 y
Spreading epileptic activity from left to right hemisphere
Wada test language function from right hemisphere

After surgery – seizures largely eliminated
Immediate aphasia
Some recovery, but language worse than before

J Neurol Neurosurg Psychiatry 2004;75:149-151
Short report
Aphasia after hemispherectomy in an adult with early onset epilepsy and hemiplegia
T Loddenkemper1, D S Dinner1, C Kubu2, R Prayson3, W Bingaman4, A Dagirmanjian5, E Wyllie1

Self-test question

How soon must a stroke sufferer get to the ER for her to get an effective drug treatment?

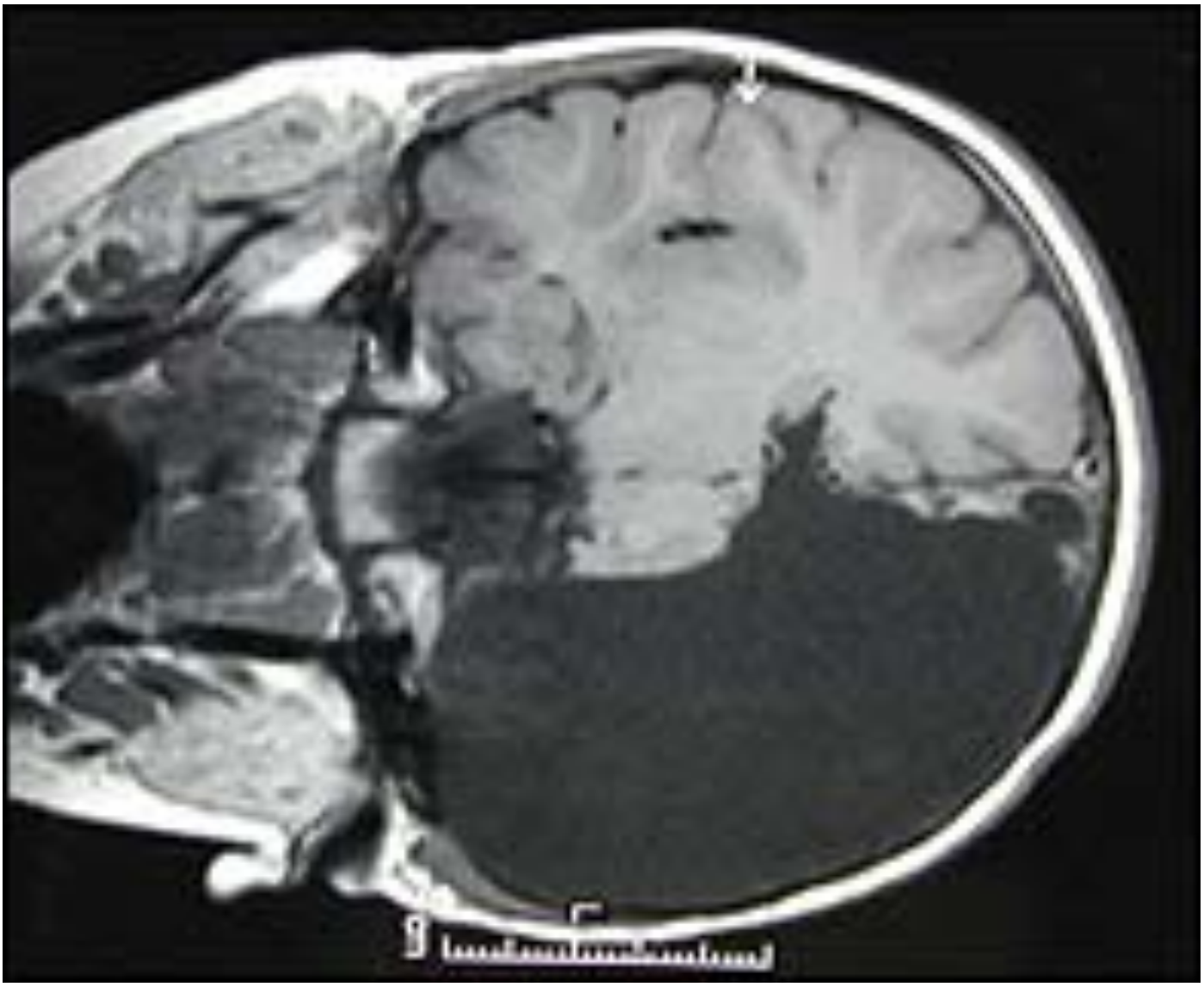
A. 30 min

B. 3 h

C. 6 h

D. 1 day

E. 2 days

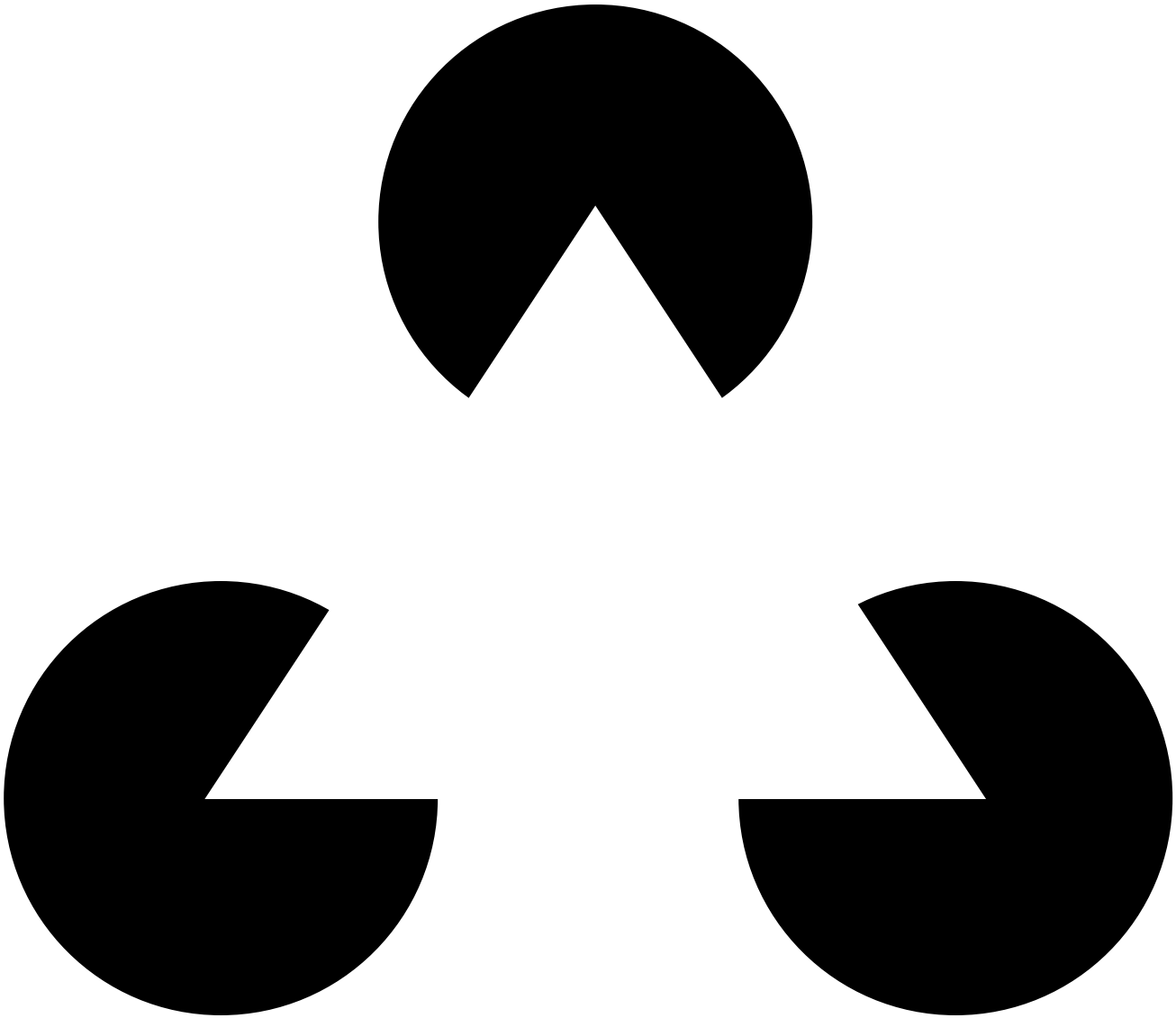


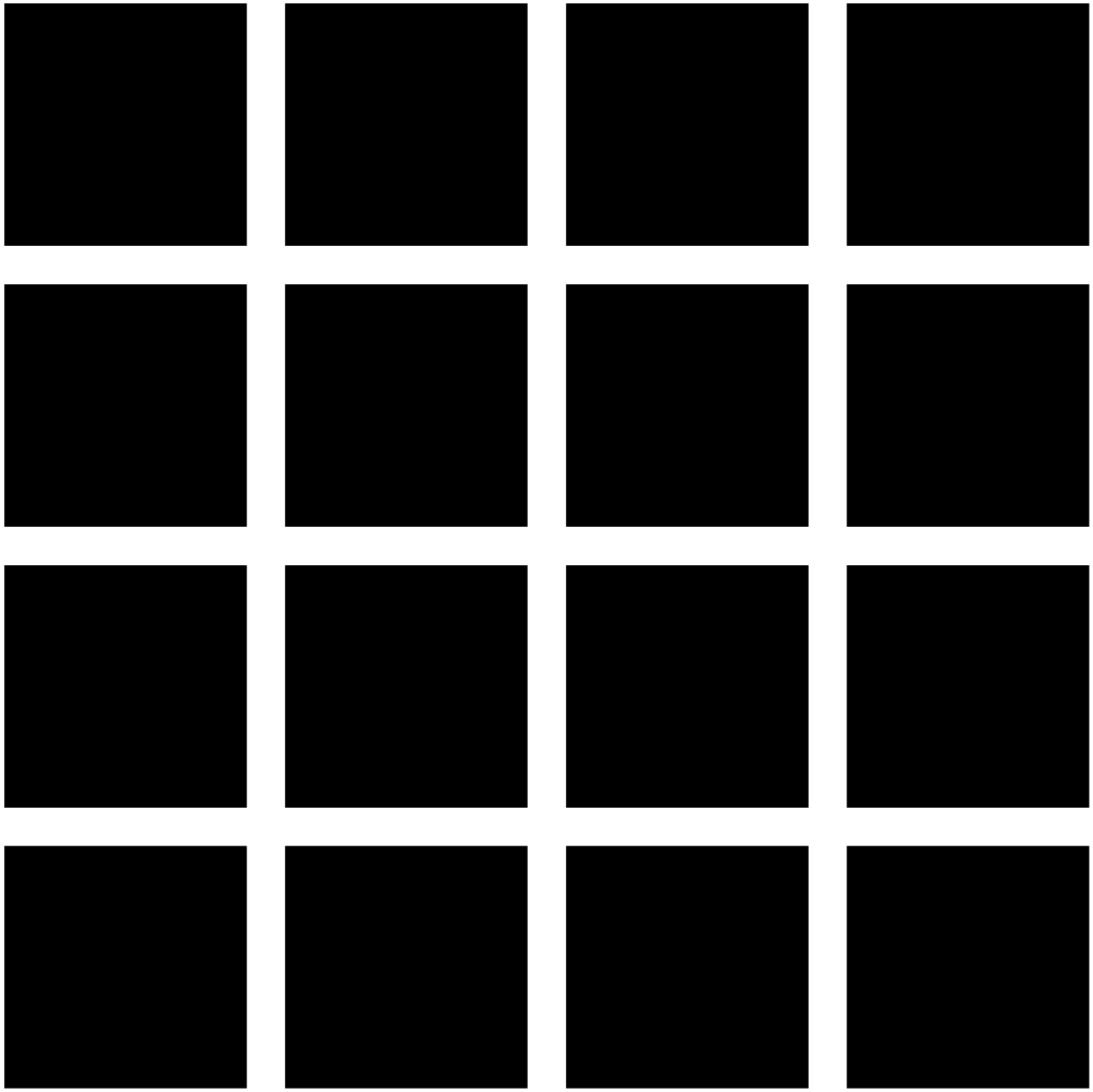
Reading: Section 7.1

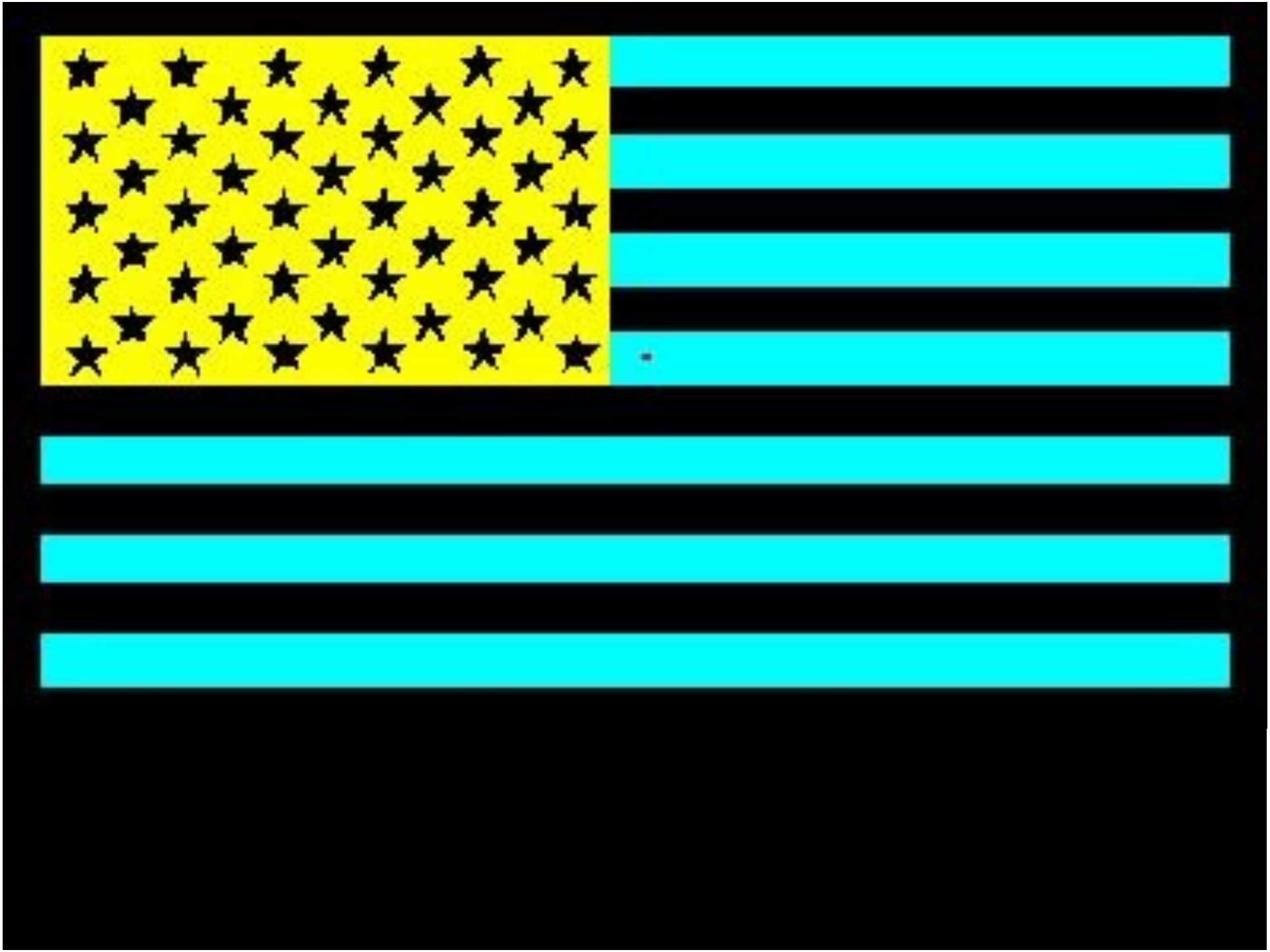
Study Questions:

1. **Define "receptive fields." How are they assessed? From this and other lectures, give several examples from different senses. Include peripheral and cortical sites.**

2. **Give several examples of how an auditory perception is derived from physical aspects of pressure waves.**







1. transduction

2. receptive fields

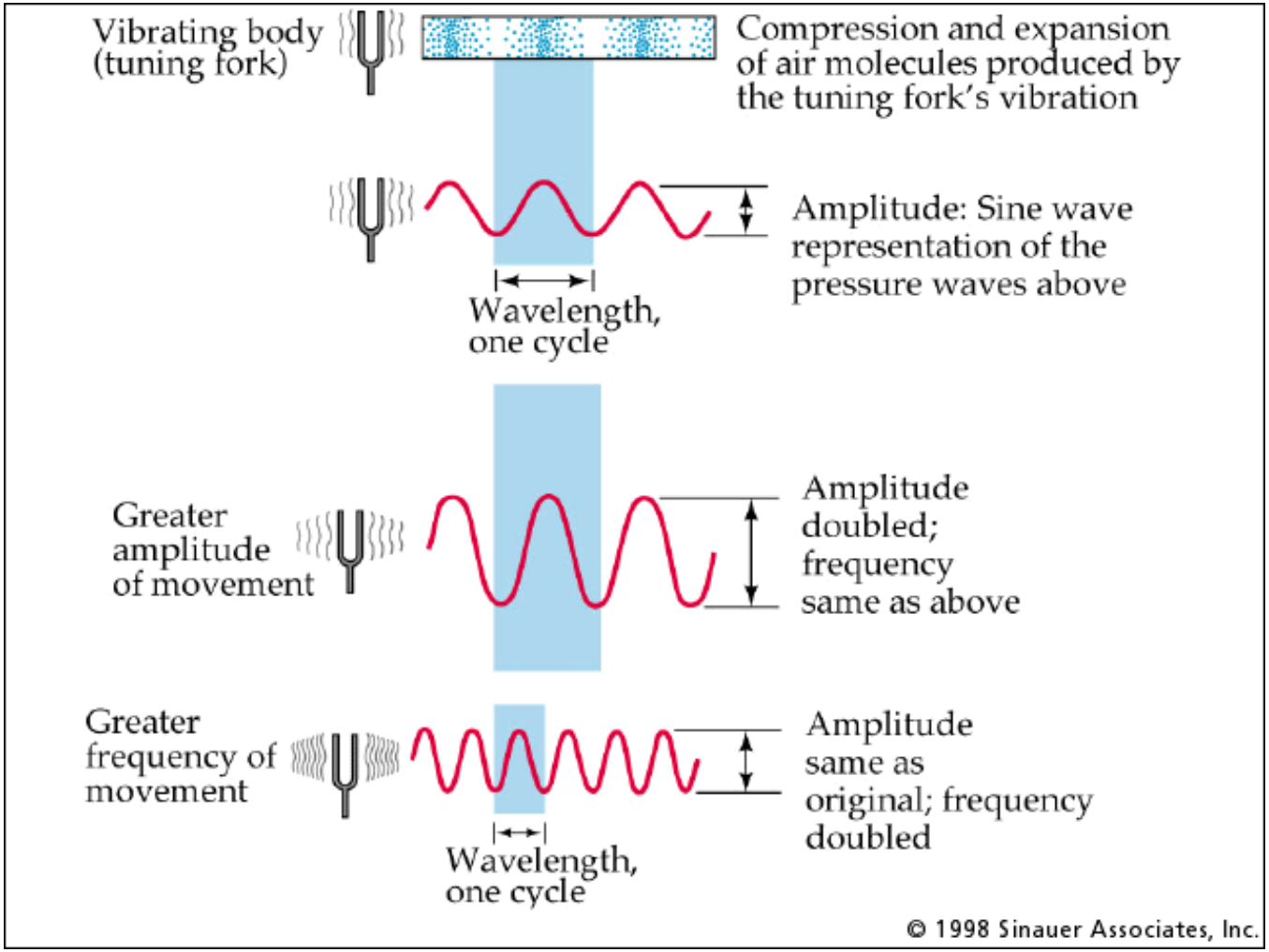
3. neural codes
    - labeled lines
    - across-fiber processing

4. hierarchical organization

5. maps/organization

6. active constructions
    - regulation of input
    - perceive things are not there

7. adaptation



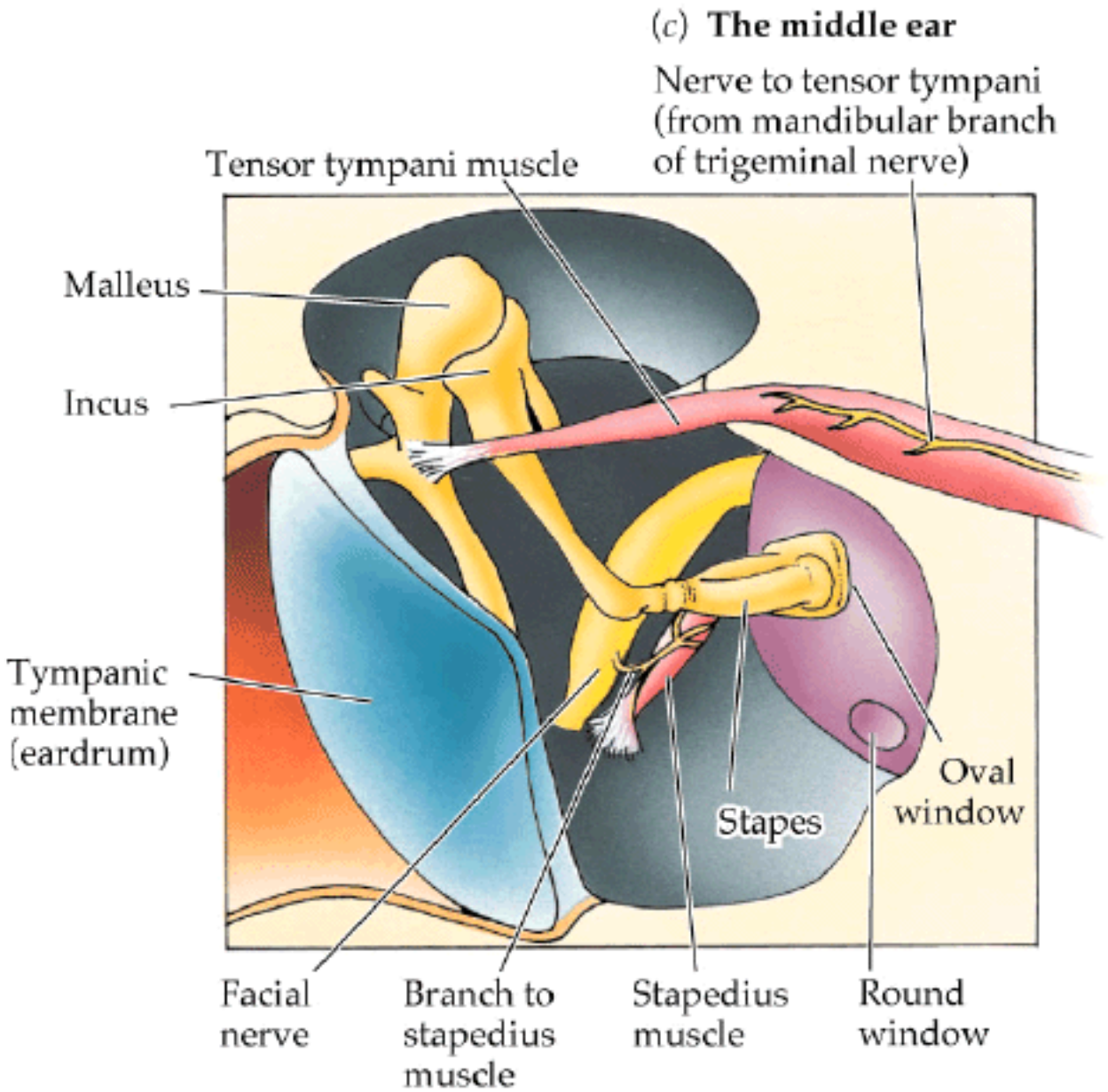
Pressure waves

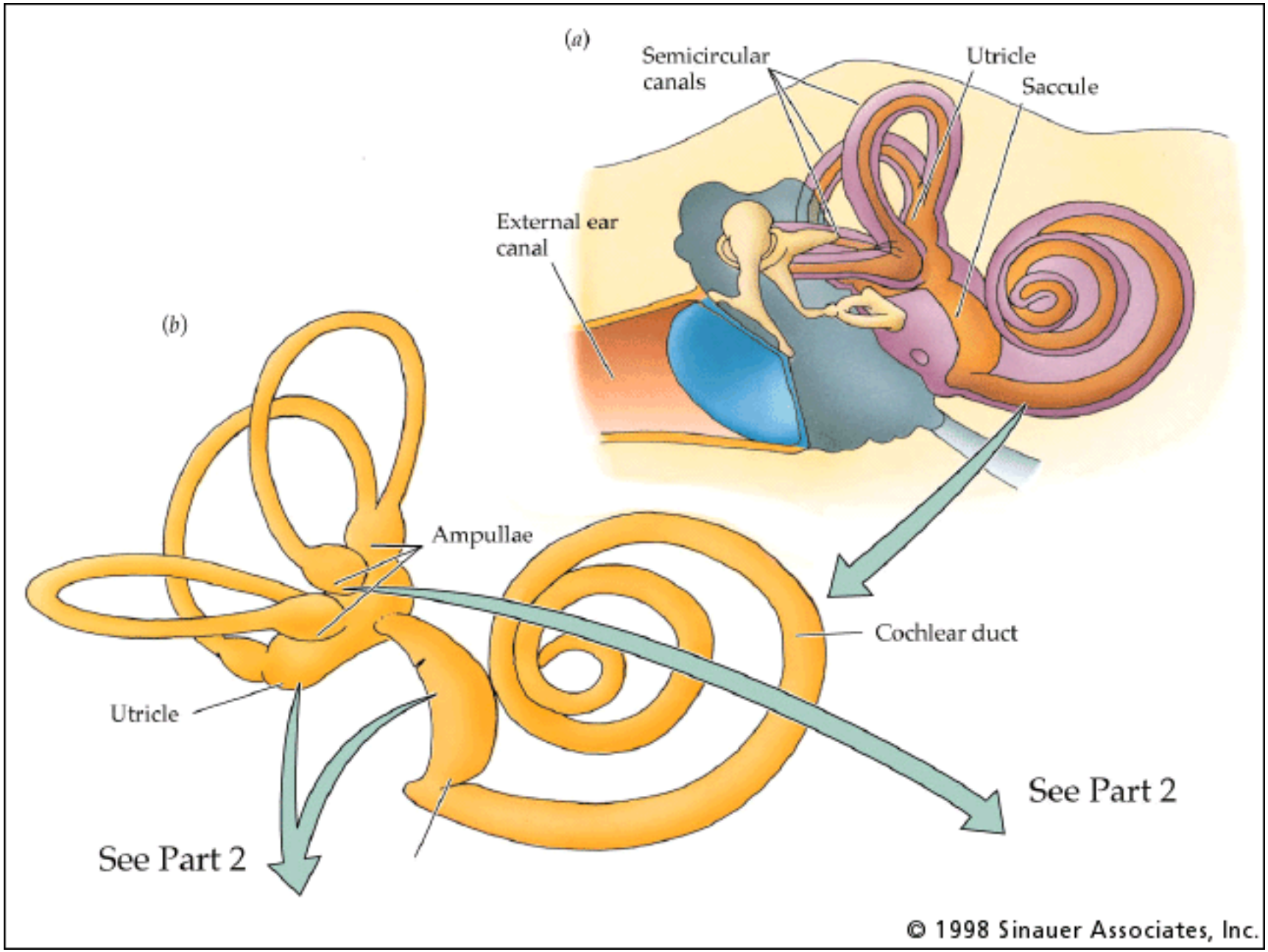
Pitch = Frequency

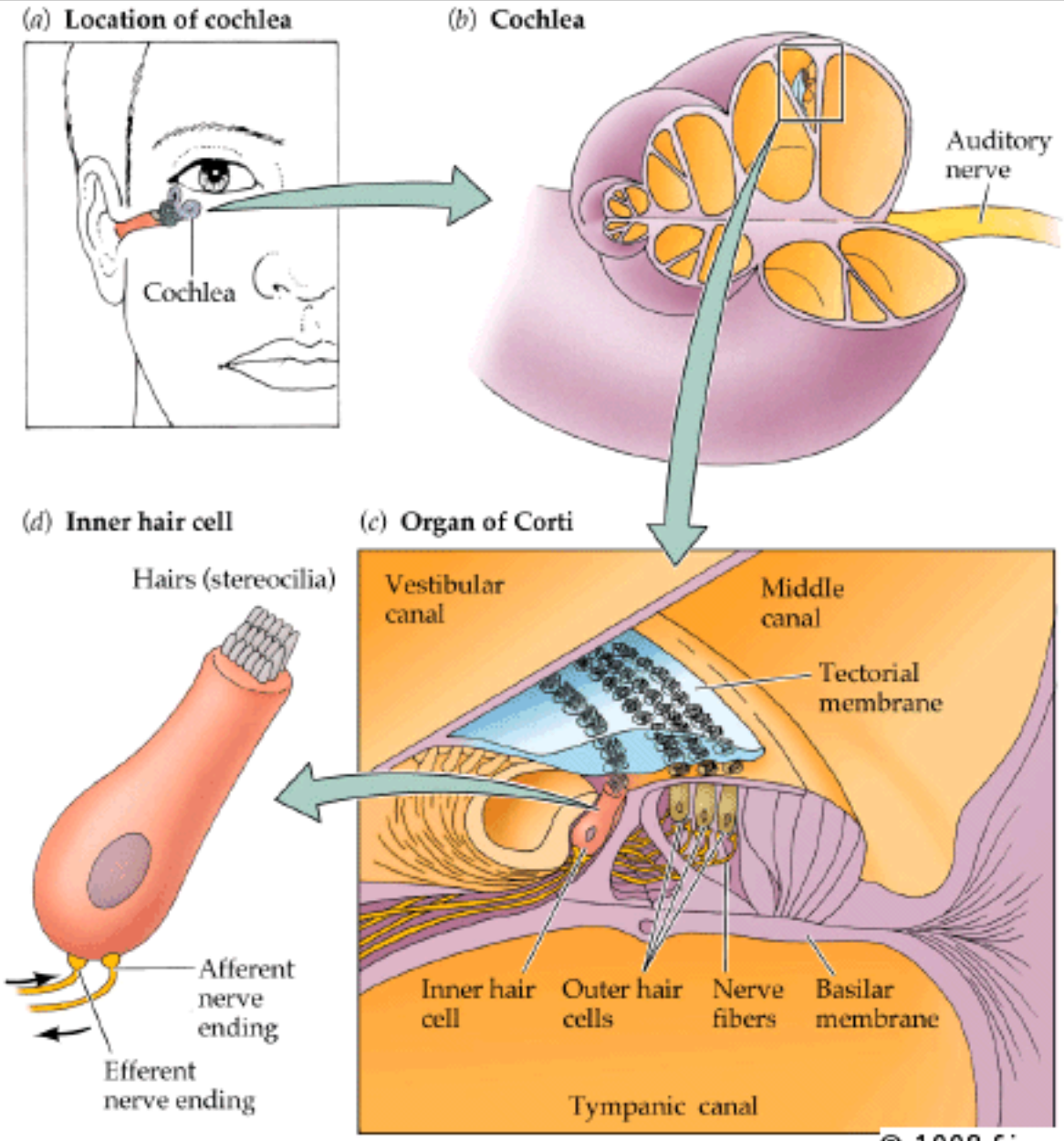
Loudness = Amplitude

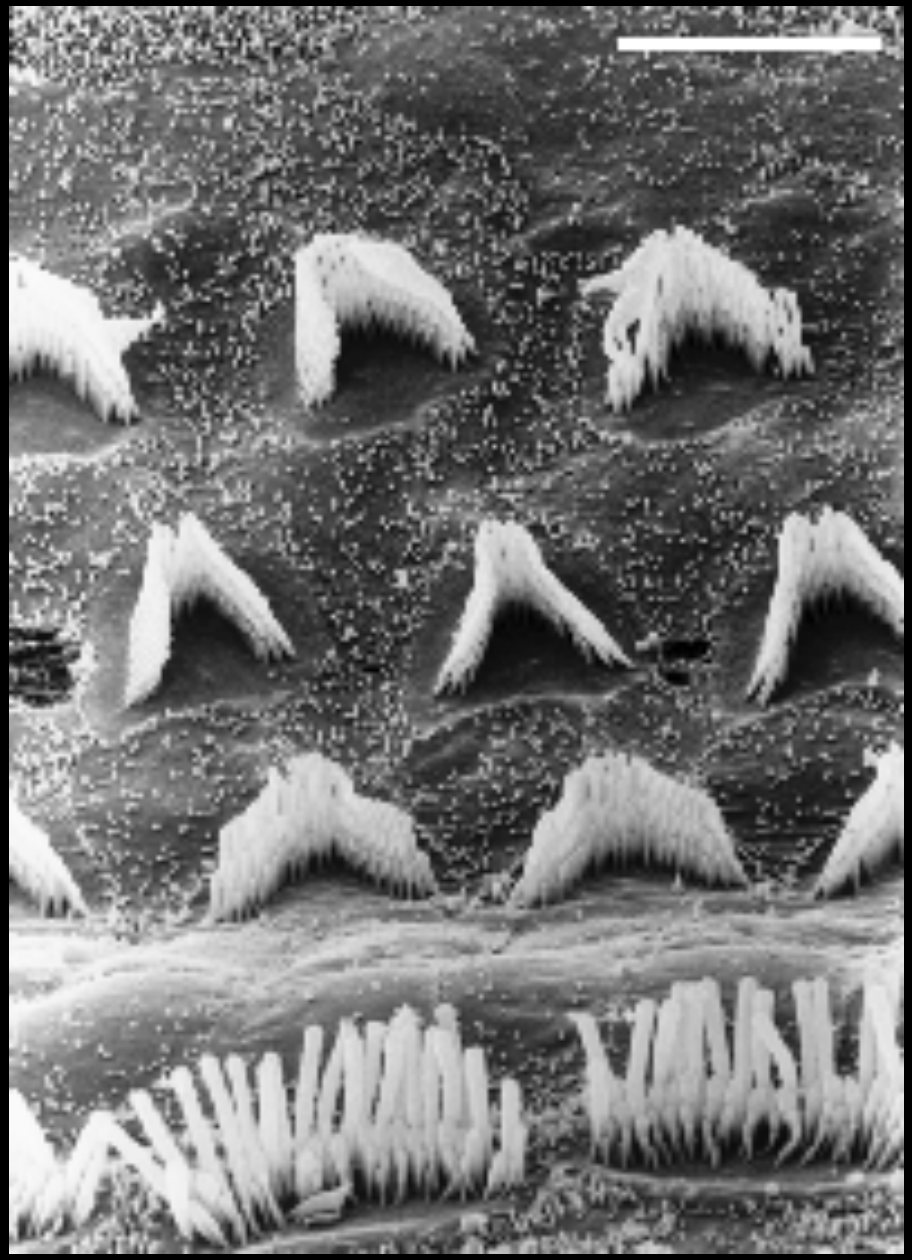
Hearing - perception of pressure (sound) waves
Vestibular Sensation - perception of gravity, acceleration

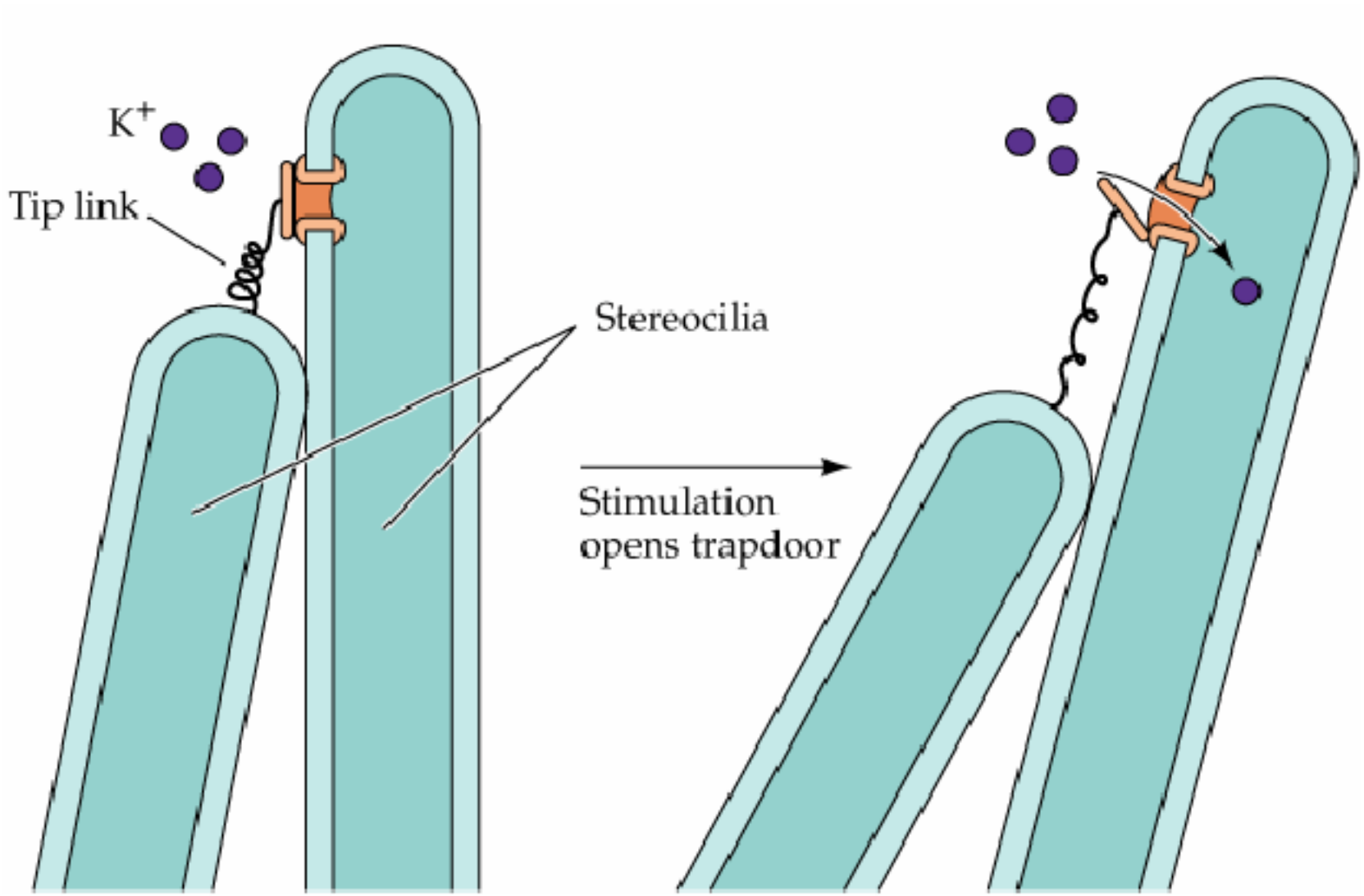
Lateral line organ
Modification for Inner Ear, Vestibular Sense?

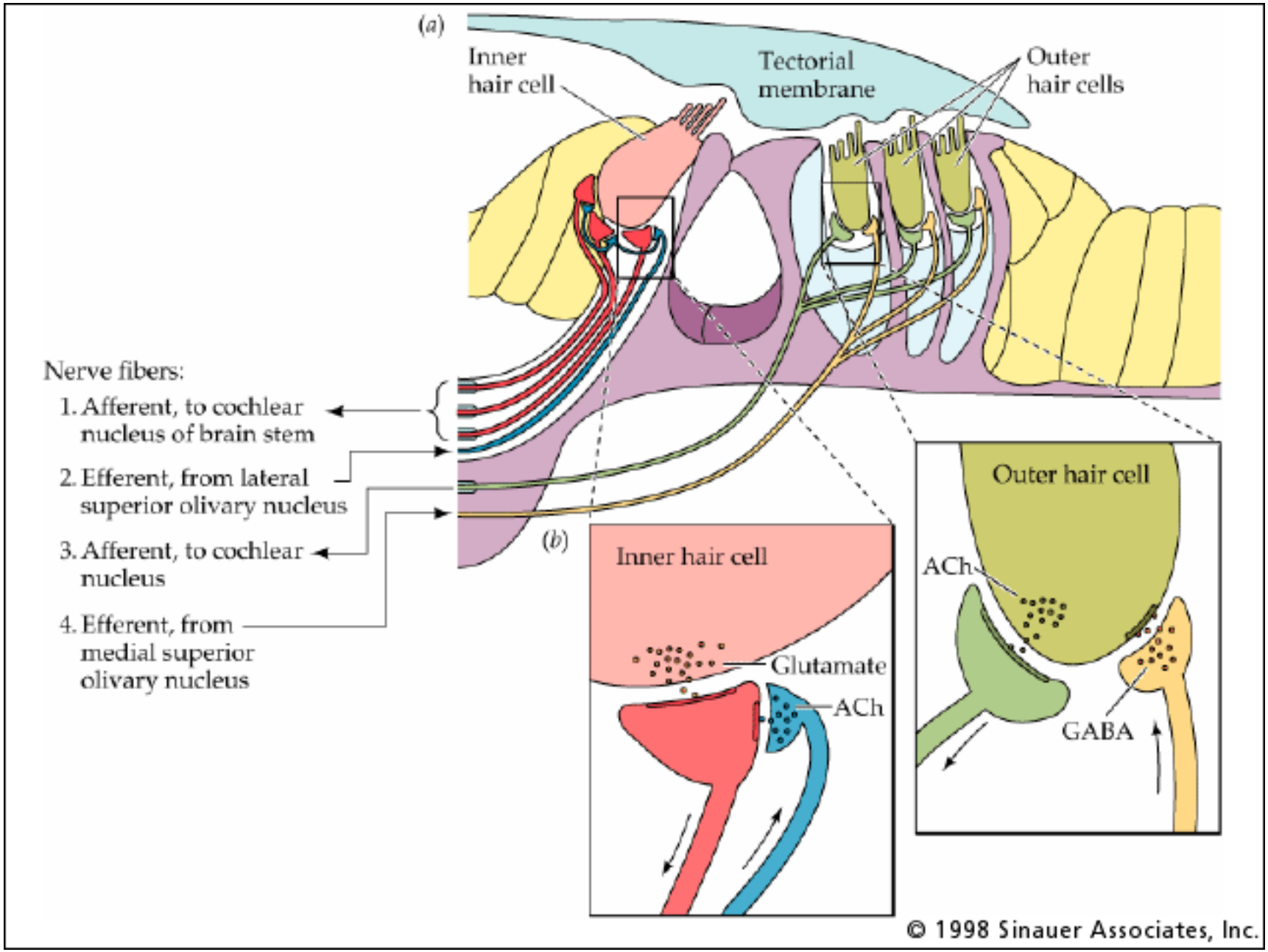


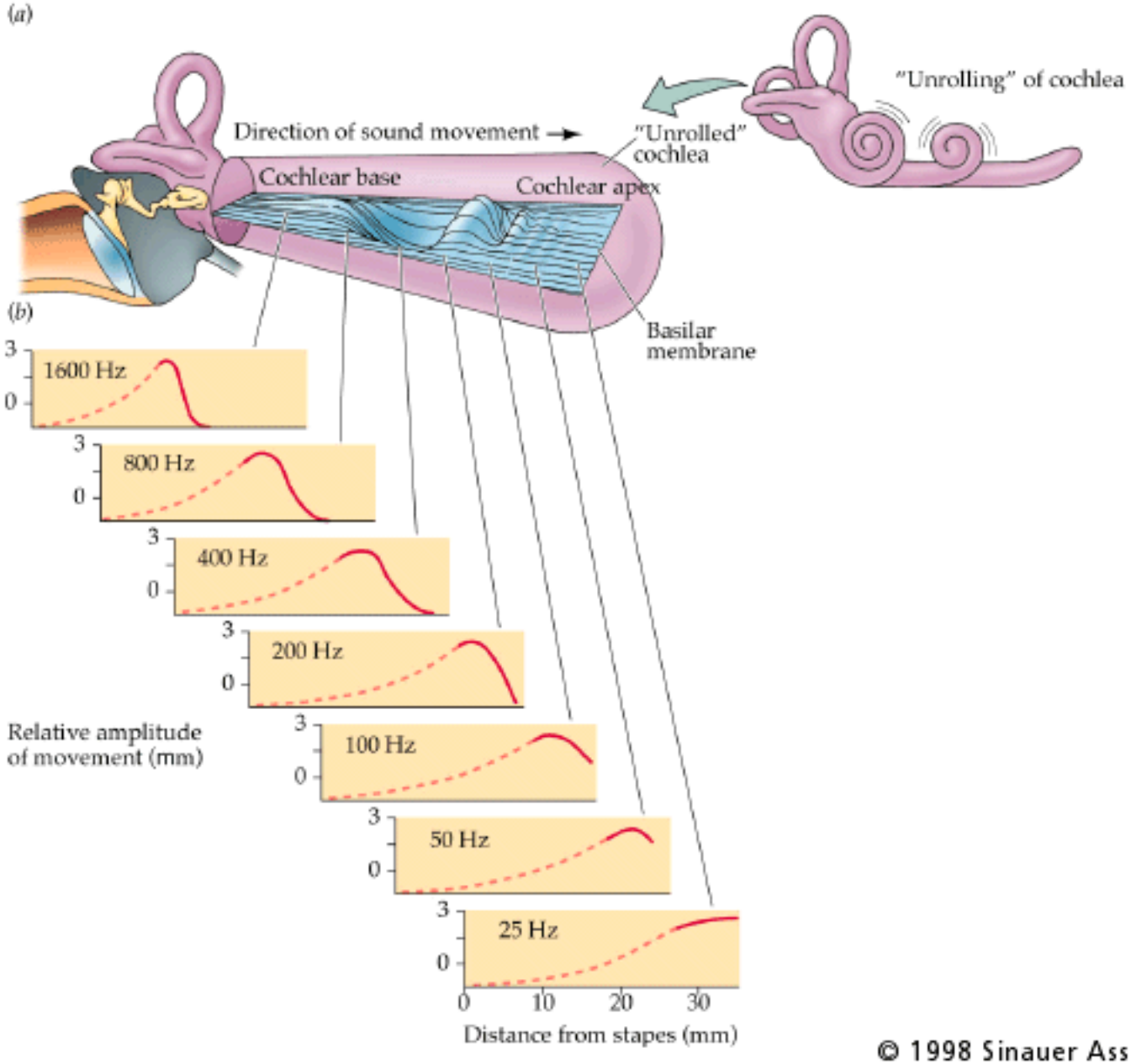




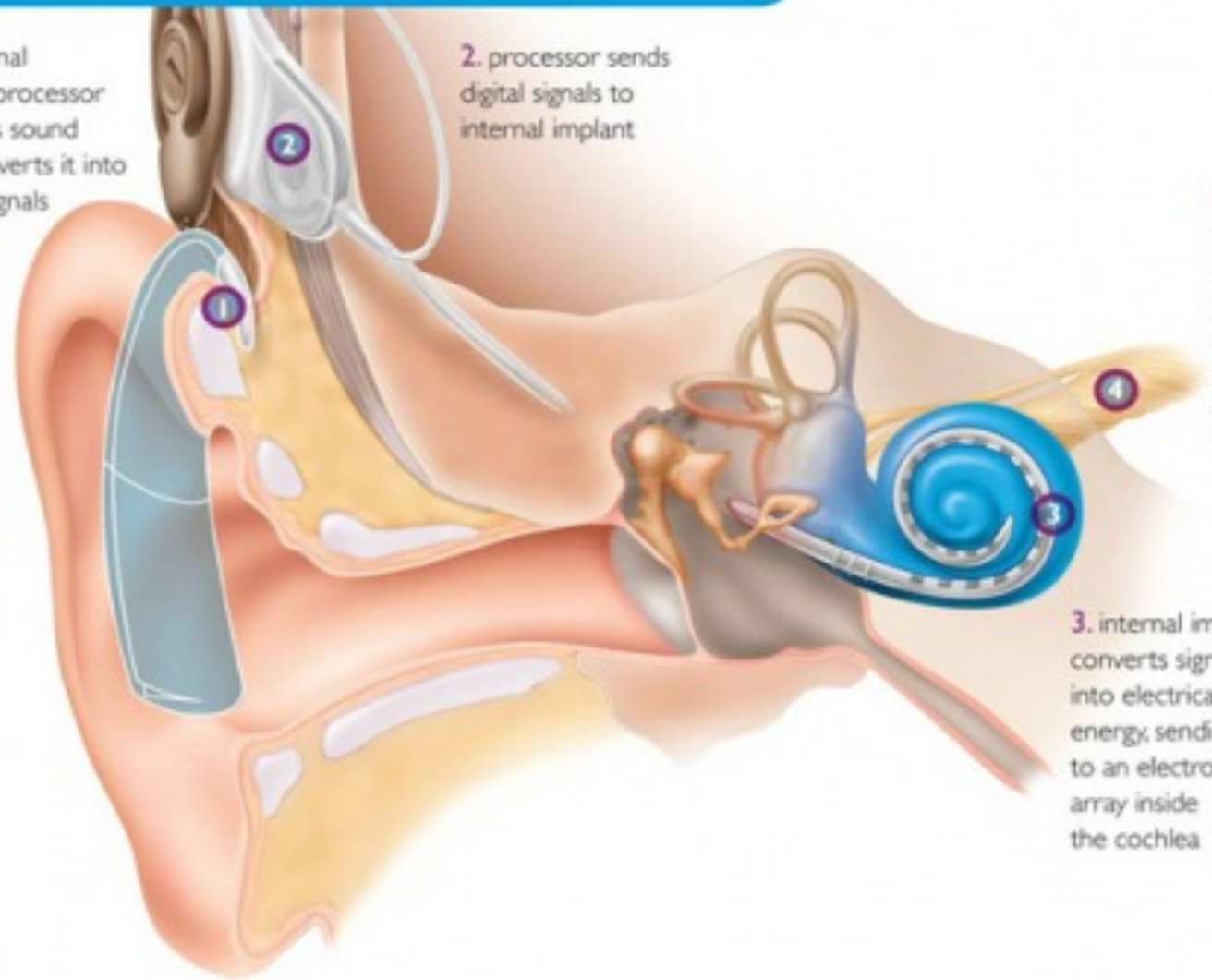


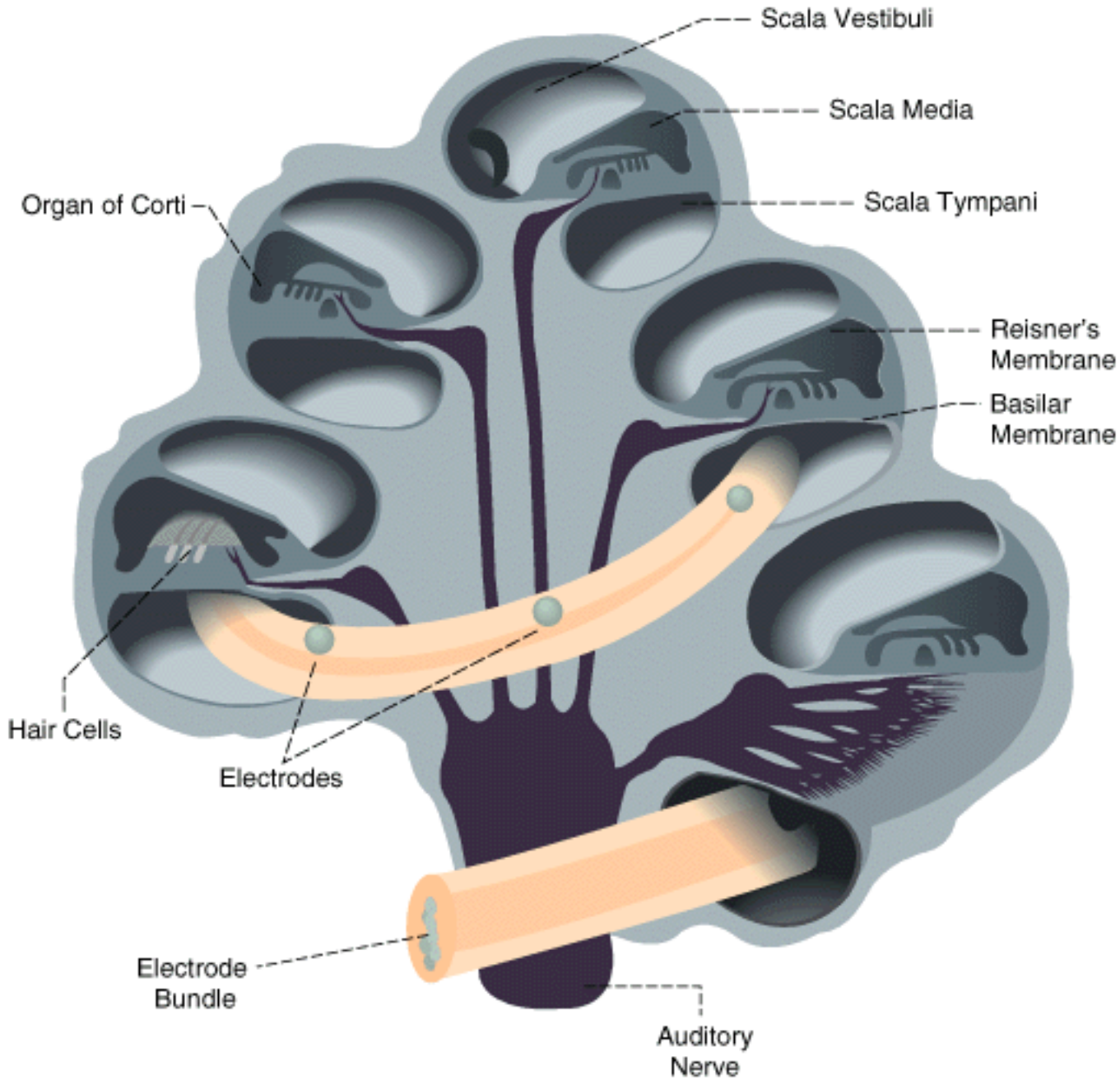


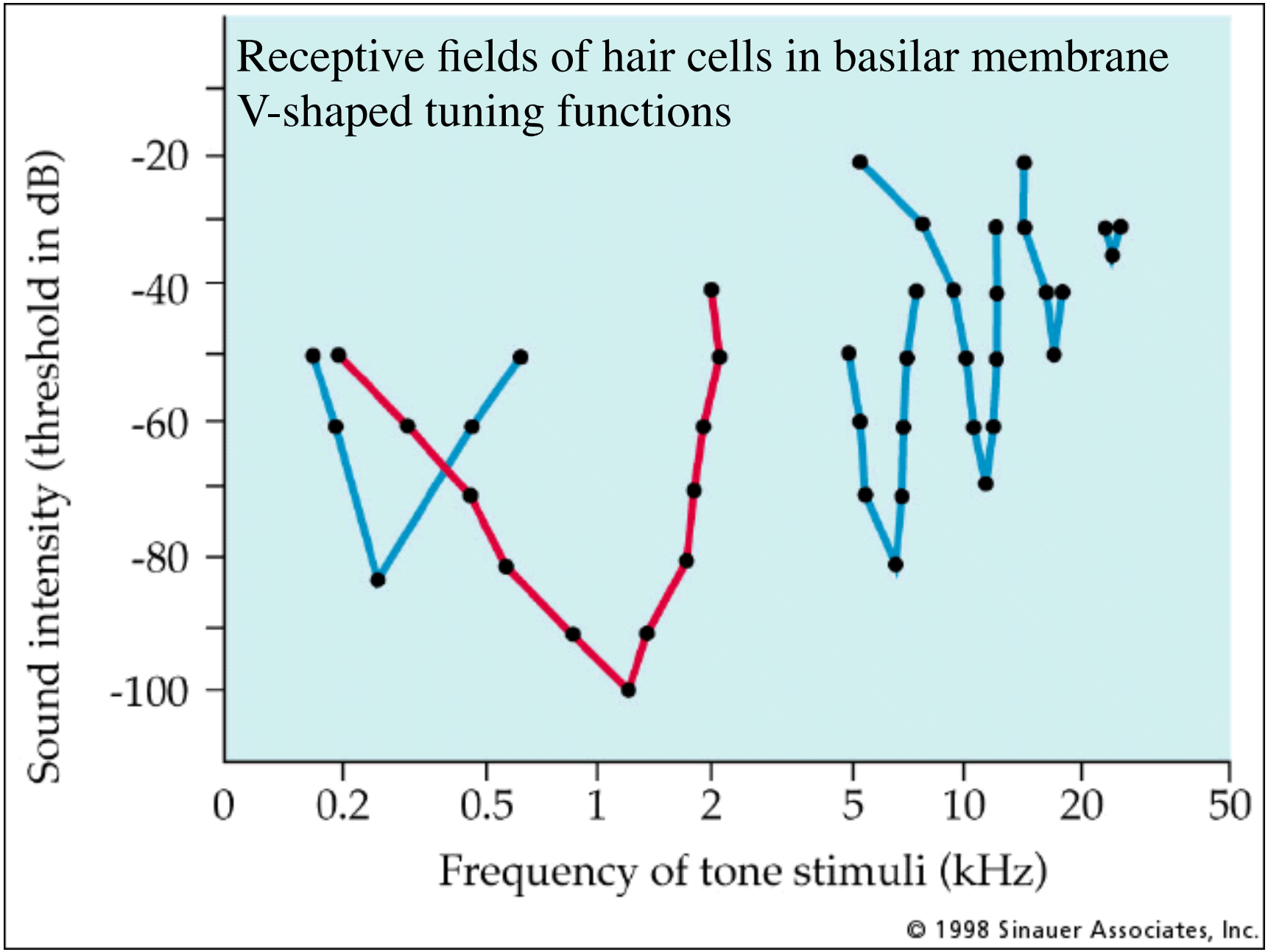


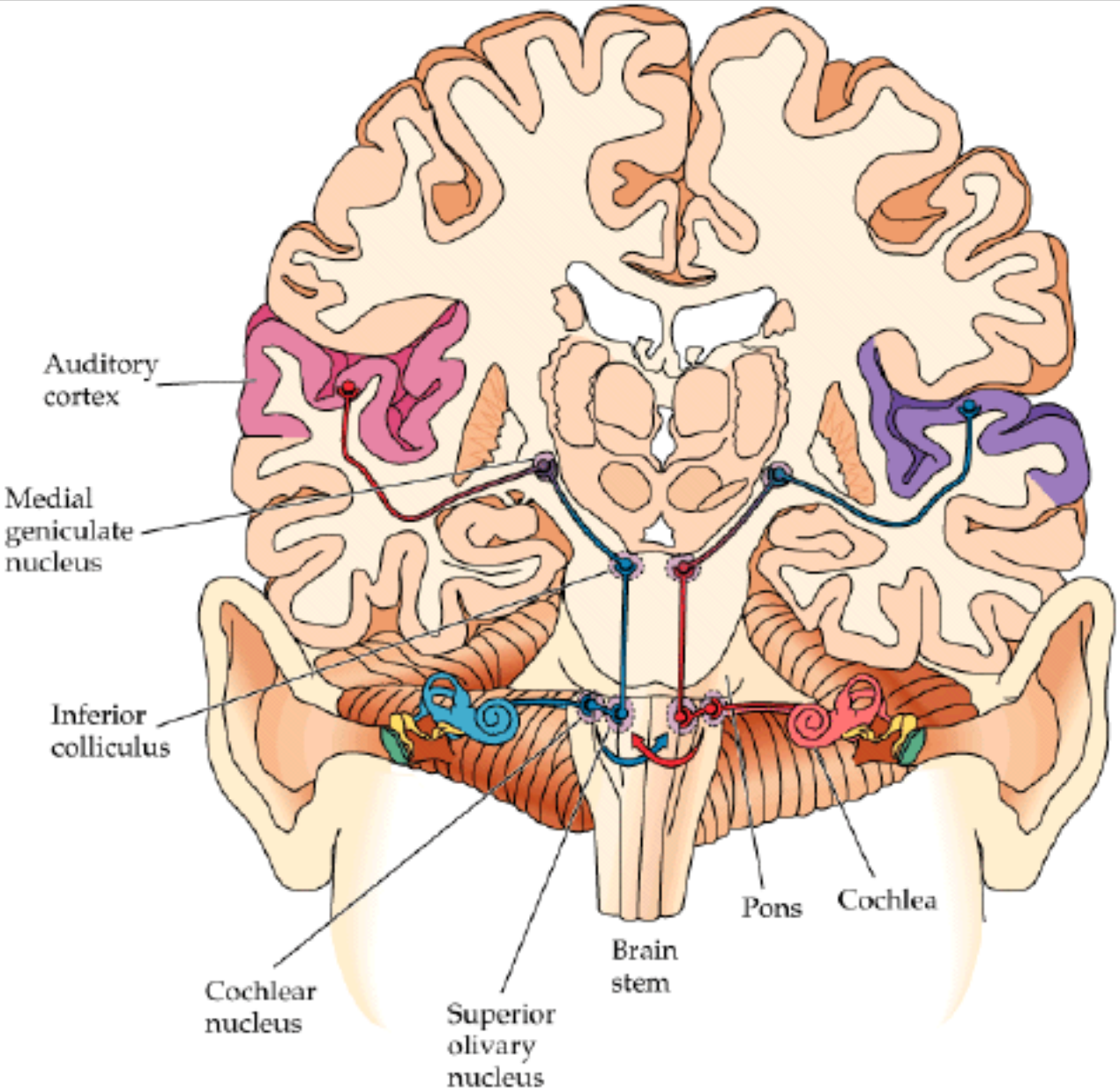


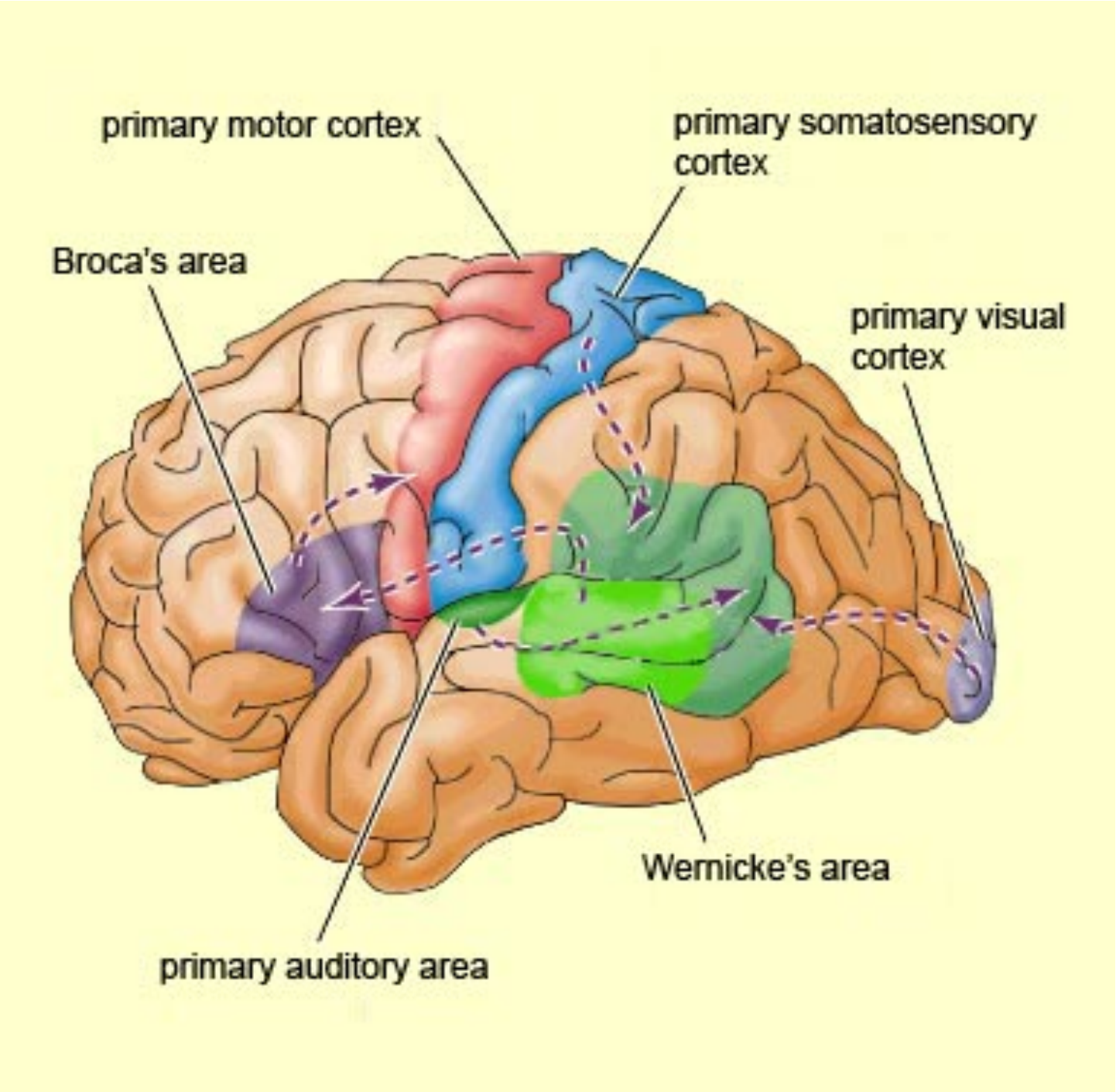
How a cochlear implant works:

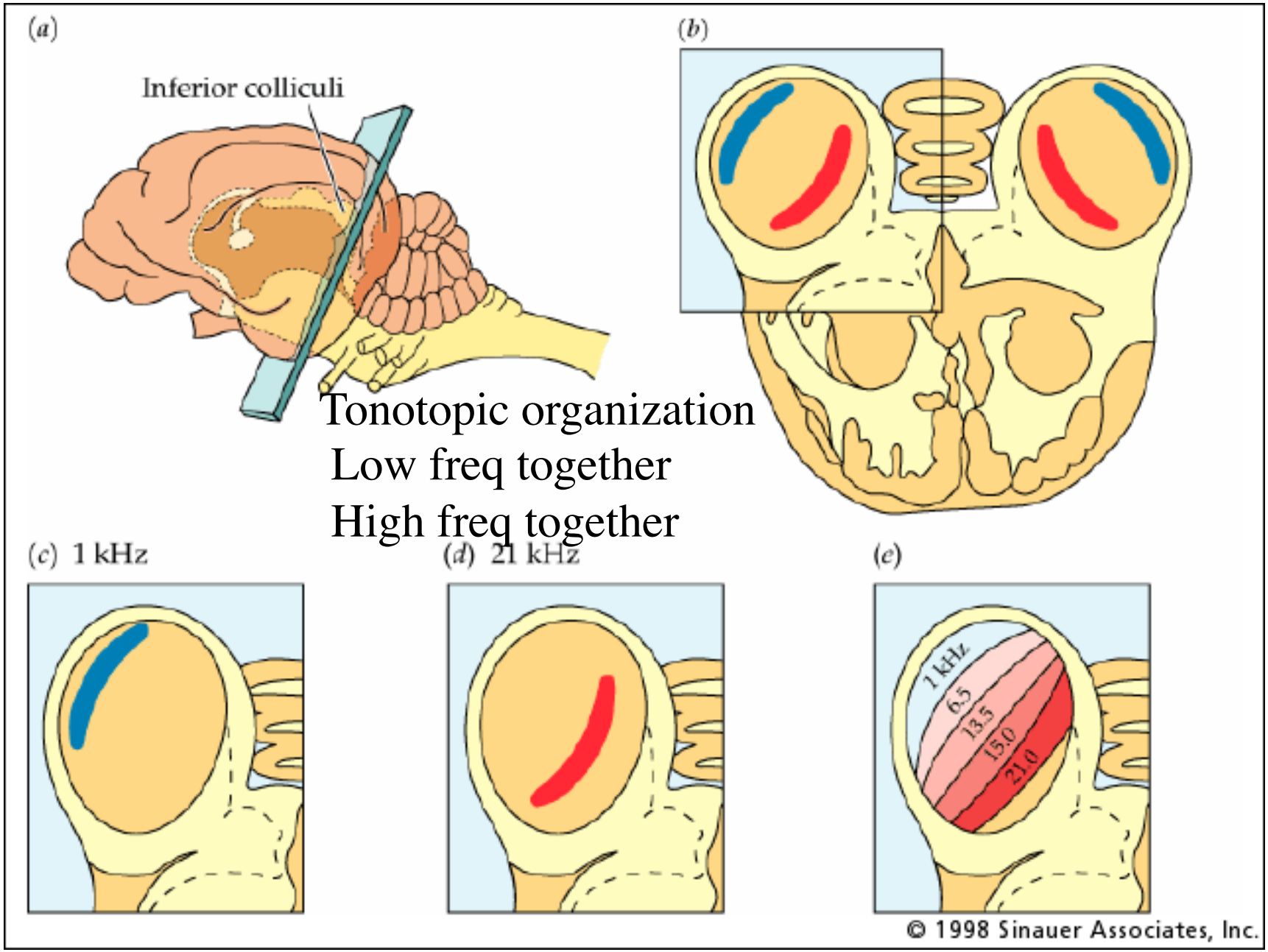



Scala Vestibuli
Scala Media
Scala Tympani
Organ of Corti
Reisner's Membrane
Basilar Membrane
Hair Cells
Electrodes
Electrode Bundle
Auditory Nerve

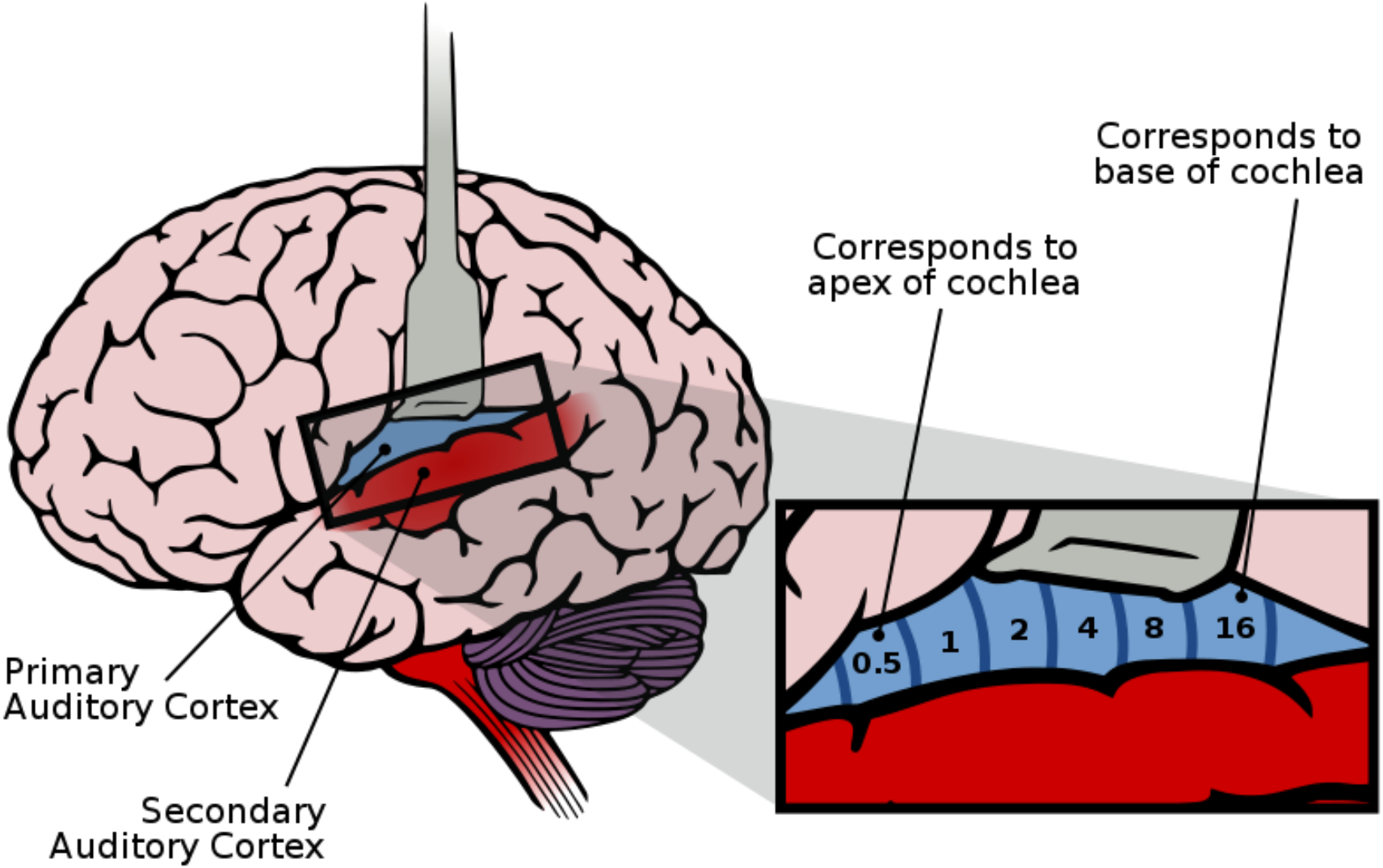

Receptive fields of hair cells in basilar membrane
V-shaped tuning functions
Sound intensity (threshold in dB)
-20
-40
-60
-80
-100
0
0.2
0.5
1
2
5
10
20
50
Frequency of tone stimuli (kHz)
© 1998 Sinauer Associates, Inc.




primary motor cortex
primary somatosensory cortex
Broca's area
primary visual cortex
Wernicke's area
primary auditory area



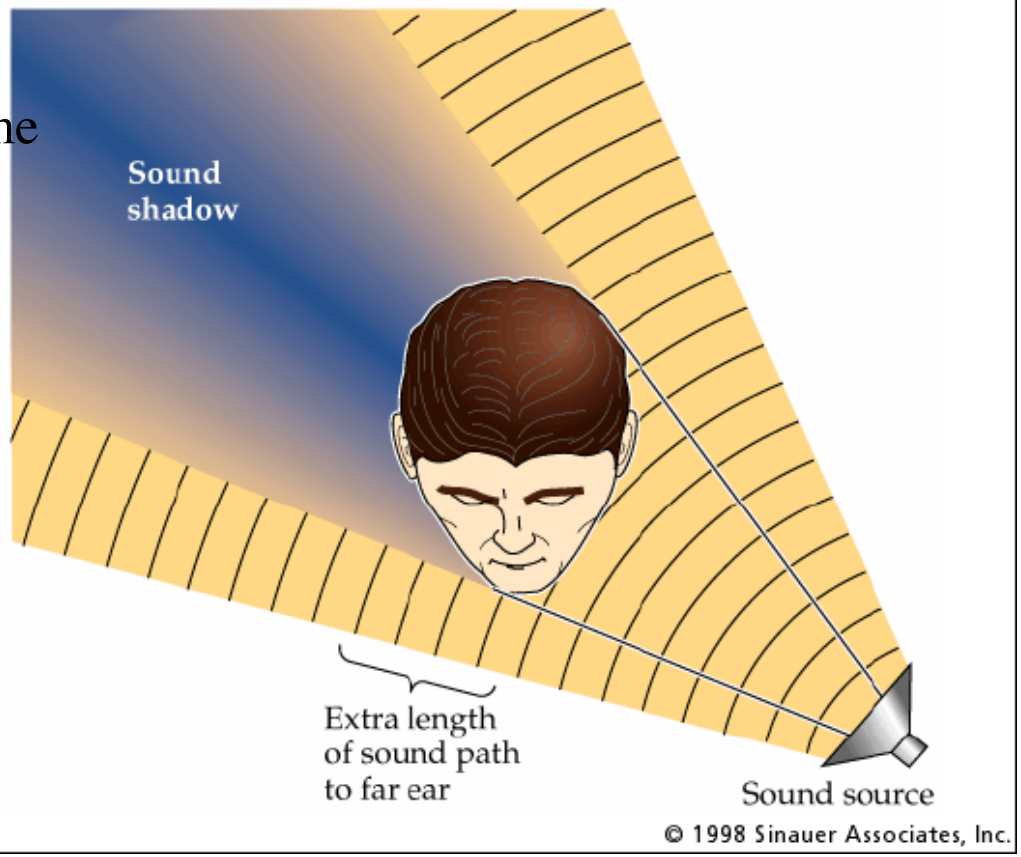
Tonotopic organization
Low freq together
High freq together

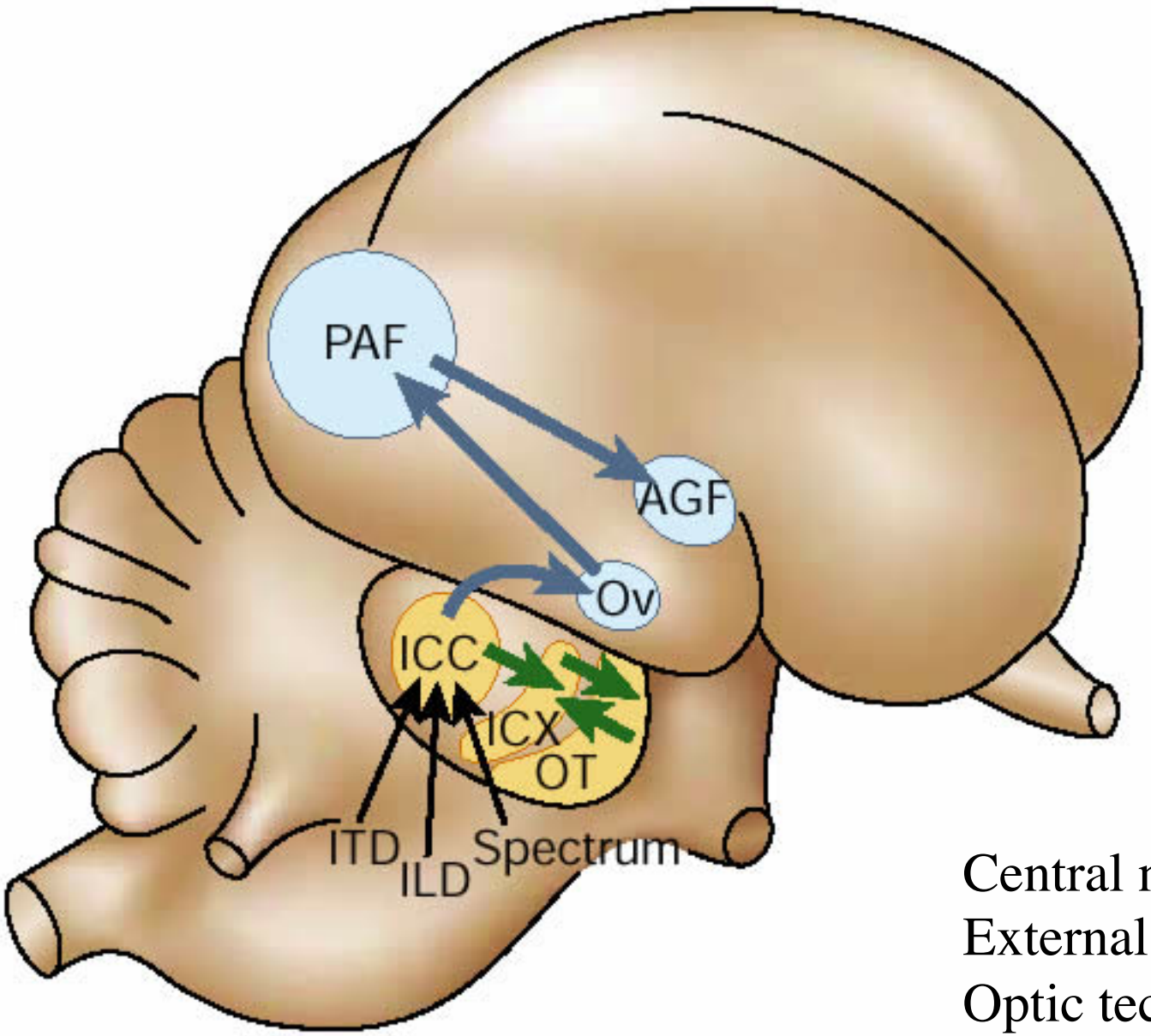

Corresponds to
base of cochlea
Corresponds to
apex of cochlea
0.5
1
2
4
8
16
Primary
Auditory Cortex
Secondary
Auditory Cortex

Auditory Localization
Multiple mechanisms - need 2 ears to do well
1. Intensity differences
 head shadow
 sound is on side where intensity is greater
 high frequencies (>2000 Hz)

2. Arrival time
 at low frequencies, intensity is same
 takes longer to get to one ear
 brain calculates difference
 best studied in owls, bats
 midbrain/brainstem

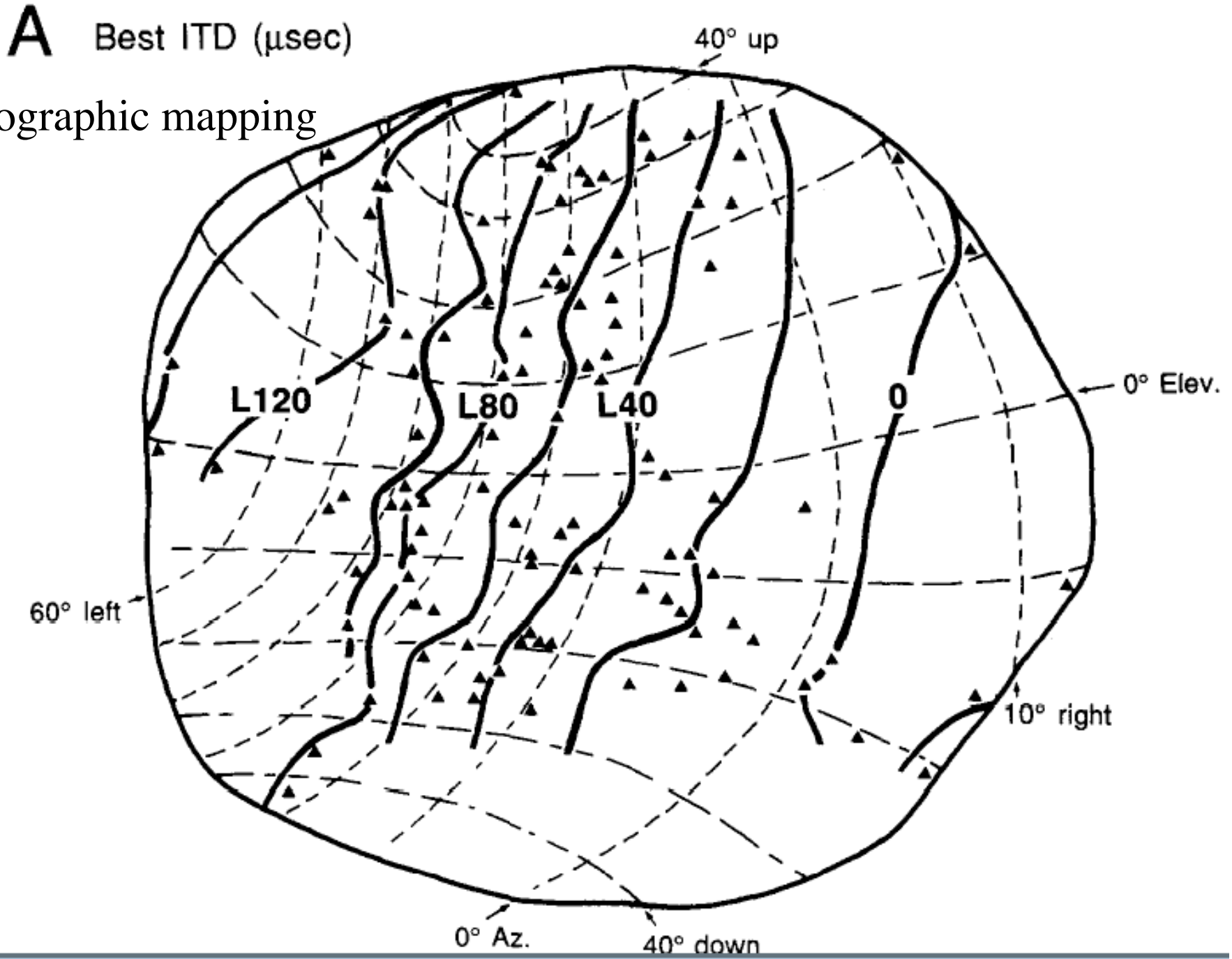
Interaural Time Differences (ITDs)

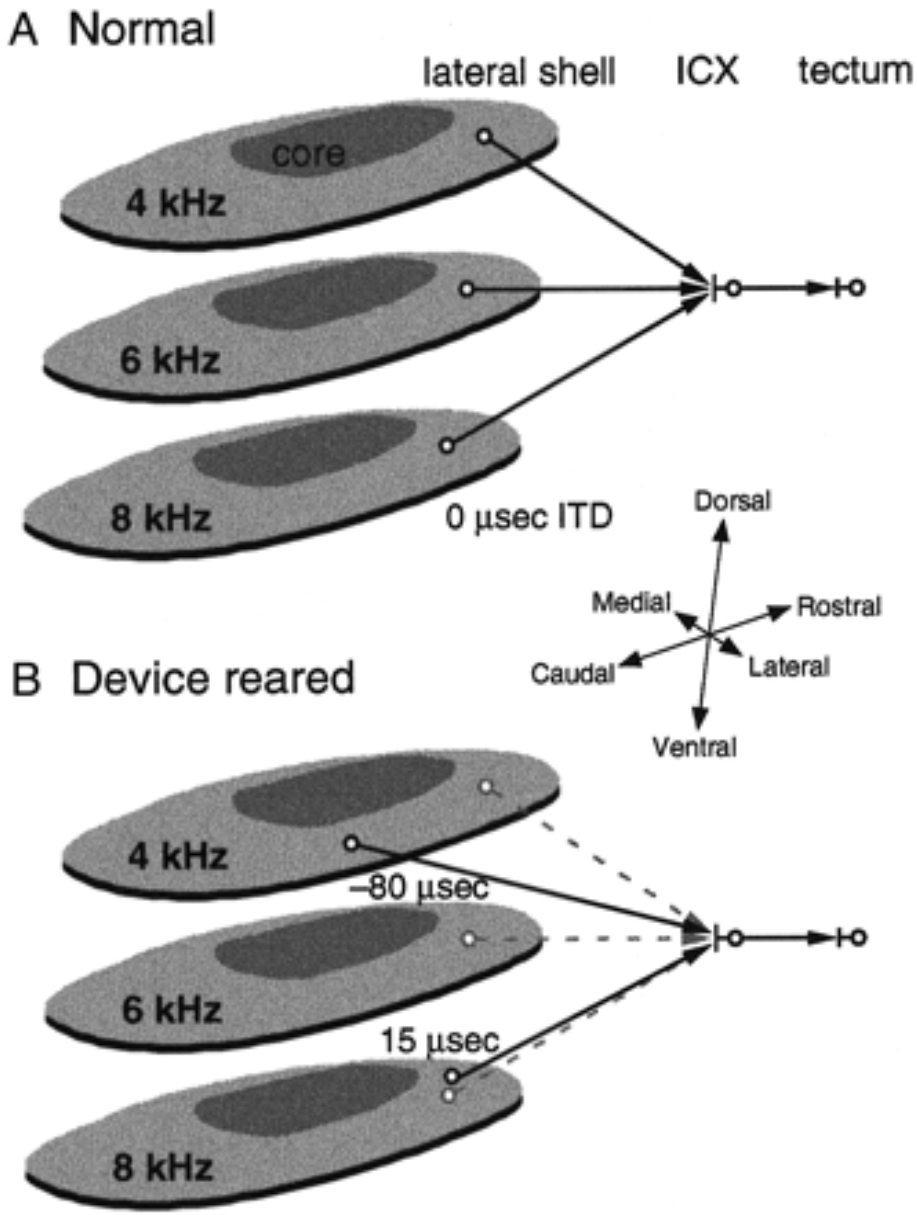




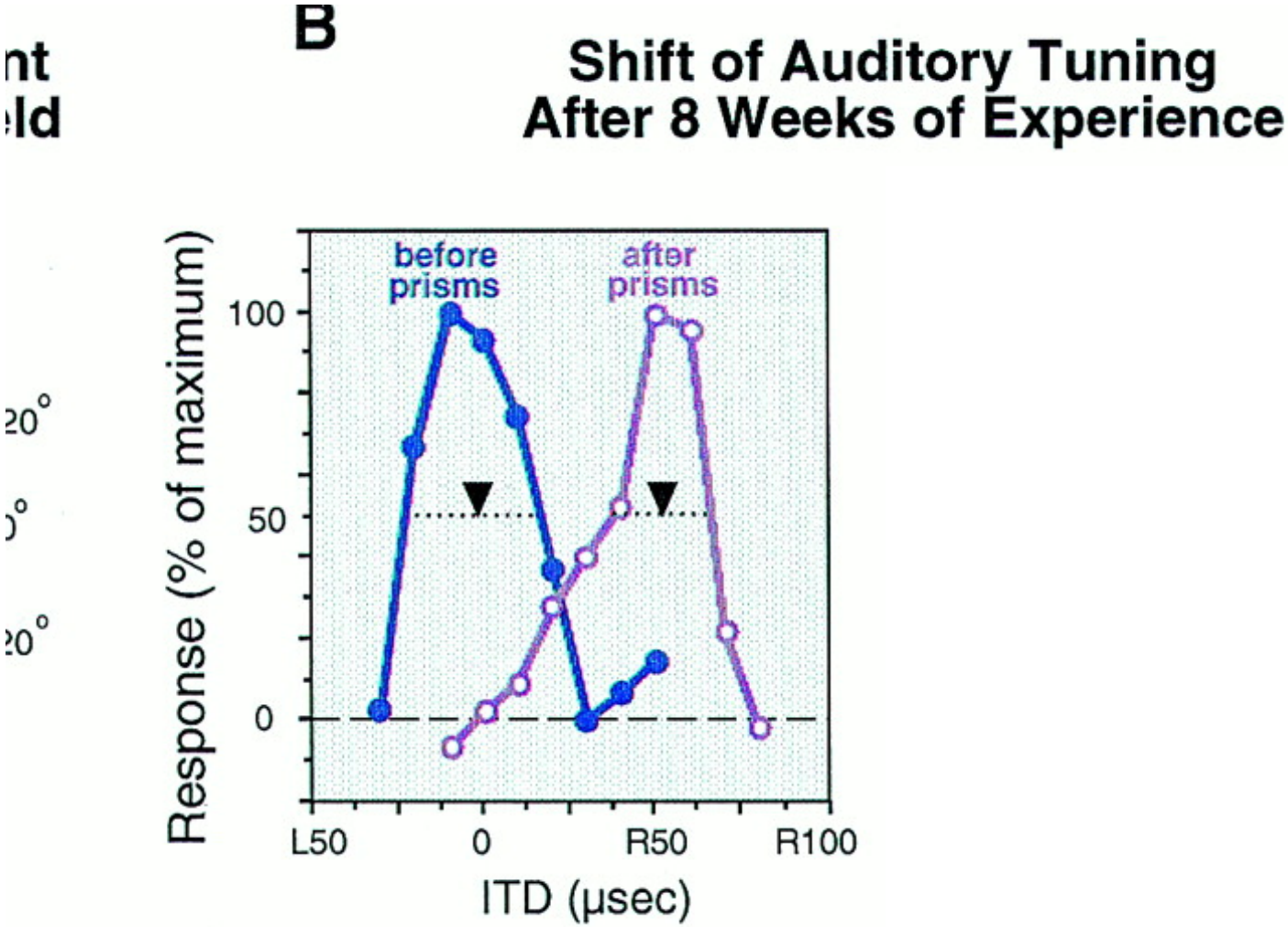
Central nuc
External nuc
Optic tectum

Topographic mapping

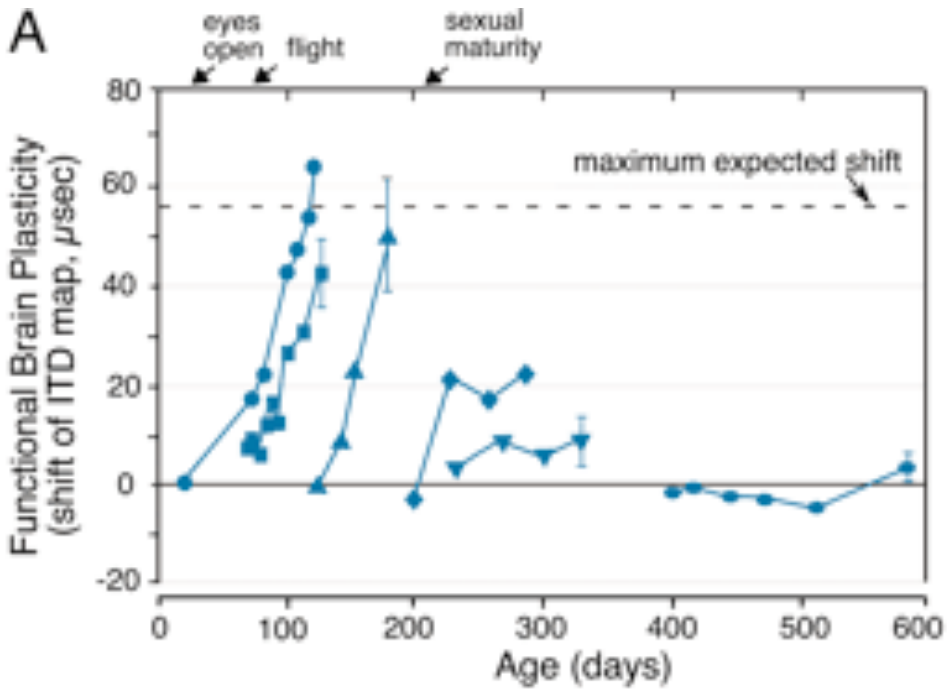




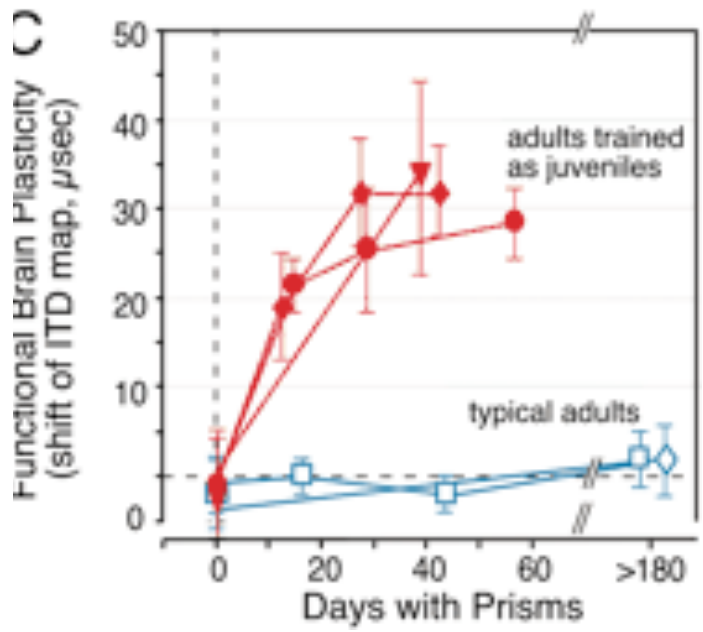
http://jn.physiology.org/content/85/4/1575.full



Knudsen E I et al. PNAS 2000;97:11815-11820



Critical period for this plasticity



Summary

1. Auditory processing occurs at several “levels”

2. Active processing of the system from “above”

3. Model systems teach us about how function emerges from function of specific neurons