Age-associated changes in the chemical senses

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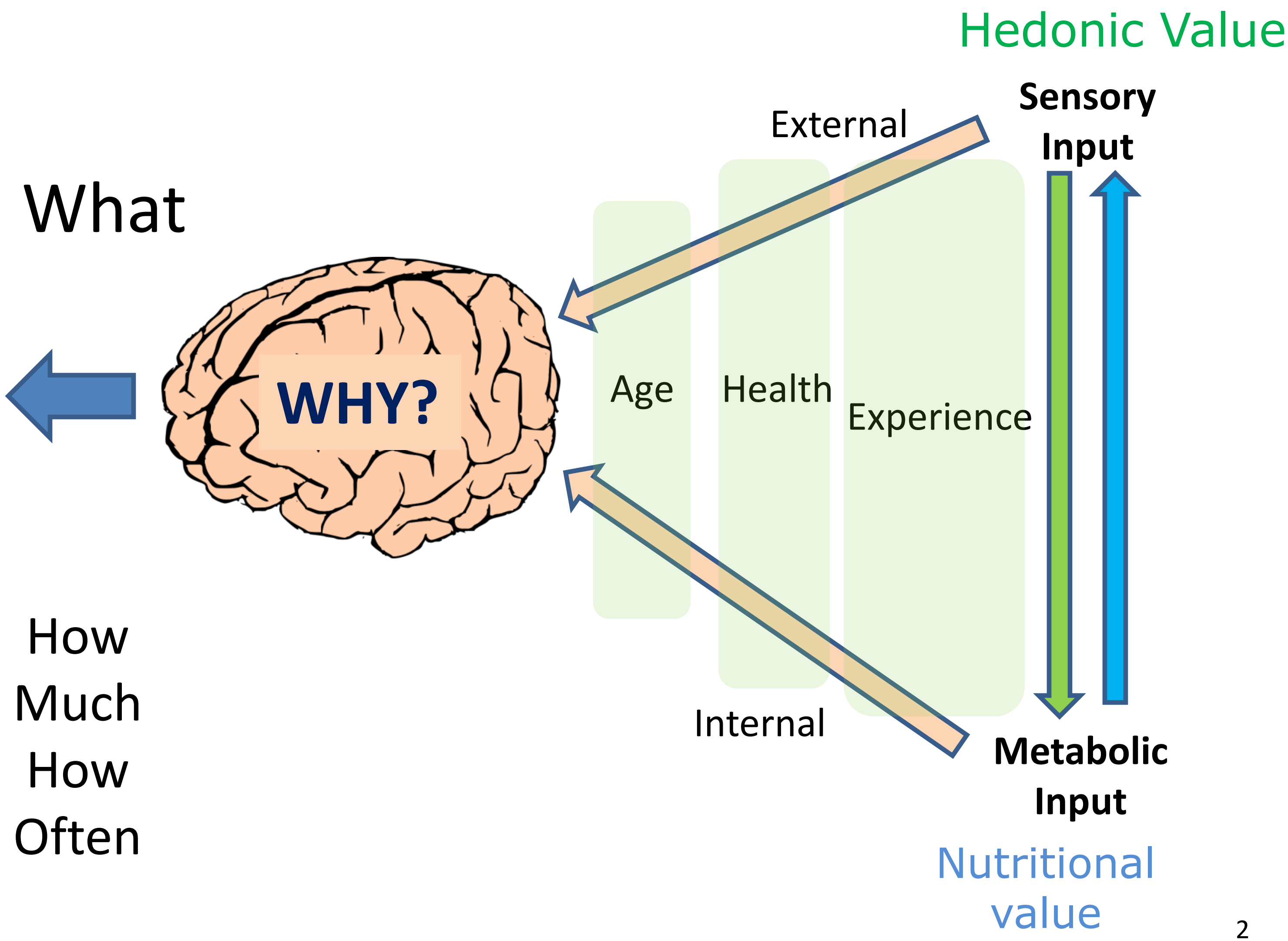
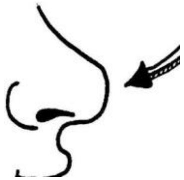
Determinants of Preference



Food Enjoyment is Multisensory

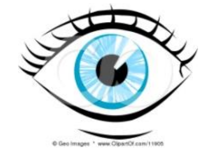


- Fruity
- Smoky
- Putrid
- Floral
- Toasty
- Musty
- Minty
- Sweet
- Sour
- Fishy
- …

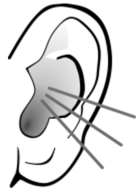
- Sweet
- Salty
- Sour
- Bitter
- Savory
- Fatty
- …

- Stinging
- Burning
- Cooling
- Warming
- Itch
- Tingling
- …

- Crispy
- Slippery
- Slimy
- Smooth
- Rough
- Chewy
- Drying
- Juicy
- Gritty
- Creamy
- …



- Color
- Shape
- Evenness
- Brightness
- …



- Crunch
- Slurp
- Snap
- Crackle
- …

All of our senses influence our responses to food

Aroma Is Key

- Few taste qualities, yet thousands of different flavors
- Odor: arguably the most informative component of flavor
  - Wintergreen vs. spearmint
  - Mango vs. peach
  - Beef vs. lamb
  - Basmati rice vs. plain rice

Olfactory loss is a risk factor for dietary inadequacy

- Blue Mountains Eye Study (Australia, 1992-94 with 5-year follow-up data)
- 1636 >49 yrs at baseline, 557 with baseline and 5-year follow-up data.
- 145-item self-administered food frequency questionnaire
- Total diet scores (TDS) reflect adherence to the Australian dietary guidelines (0 – 2) based on food intake and optimal choice

Gopinath et al., 2016

Olfactory deficits & TDS

Table 3 Longitudinal association between olfactory impairment and total diet score (TDS) in the BMES over 5 years, presented as adjusted means (SE)

Moderate/Severe olfactory impairment at baseline was significantly associated with a lower TDS at 5-year follow-up

	Age–sex-adjusted mean TDS score (SE)	Multivariable-adjusted mean TDS score (SE)[a]
Presence of olfactory impairment		
None, $n = 468$	9.93 (0.10)	9.94 (0.10)
Any, $n = 89$	9.62 (0.23)	9.63 (0.10)
p value	0.23	0.24
Severity of olfactory impairment		
None, $n = 468$	9.93 (0.10)	9.94 (0.10)
Mild, $n = 59$	9.87 (0.28)	9.89 (0.29)
Moderate/severe, $n = 30$	9.12 (0.40)*	9.09 (0.40)**
p for trend	0.09	0.08

* $p = 0.05$

** $p = 0.04$

[a] Adjusted for age, sex, education, receipt of pension, living alone, and body mass index

Gopinath et al., 2016

Epidemiology of Hearing Loss Study

Schubert et al., 2016

Hearing, visual acuity, and olfaction

n = 2,418, aged 53-97 yrs (mean = 69 yrs)

17-year follow-up (mean = 12.8 yrs) mortality

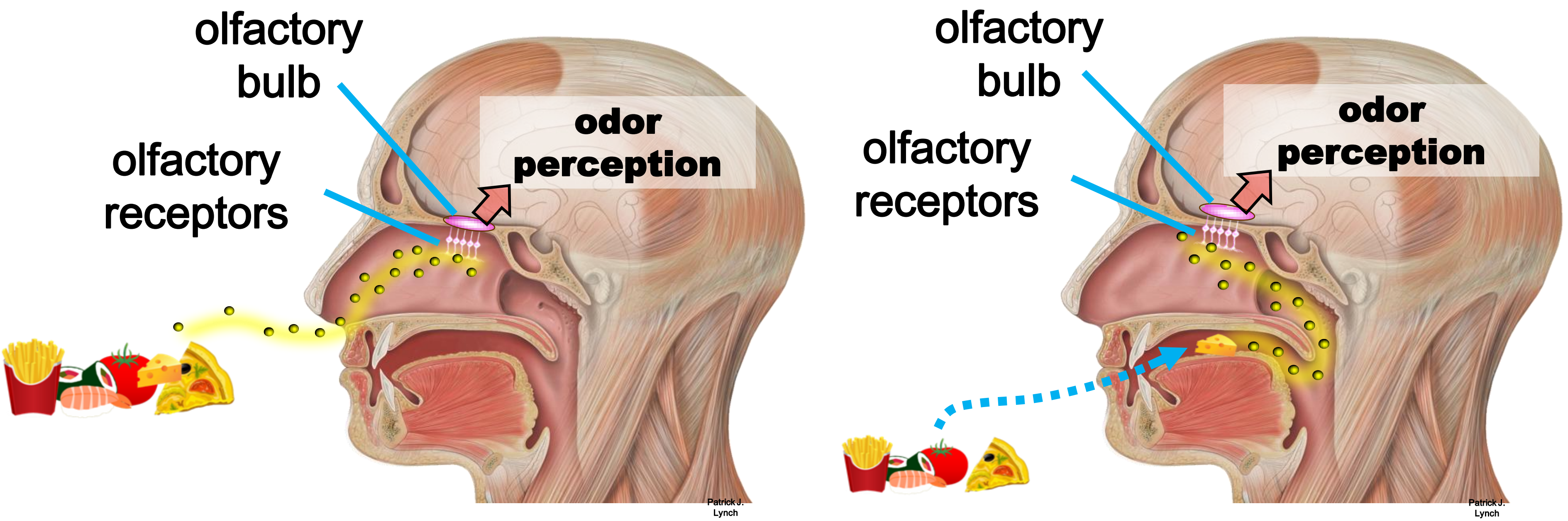
CONCLUSION

Olfactory impairment, but not hearing or visual impairment, was significantly associated with an increased risk of mortality. These results suggest that olfactory impairment may be a marker of underlying physiologic processes or pathology that is associated with aging and reduced survival in older adults.

- Data were adjusted for age, sex, sensory co-morbidities, CVD, cognitive impairment, frailty, subclinical atherosclerosis and inflammatory marker levels

Olfaction in Flavor Perception

- The "Taste" of food relies on both ortho- and retro-nasal olfaction



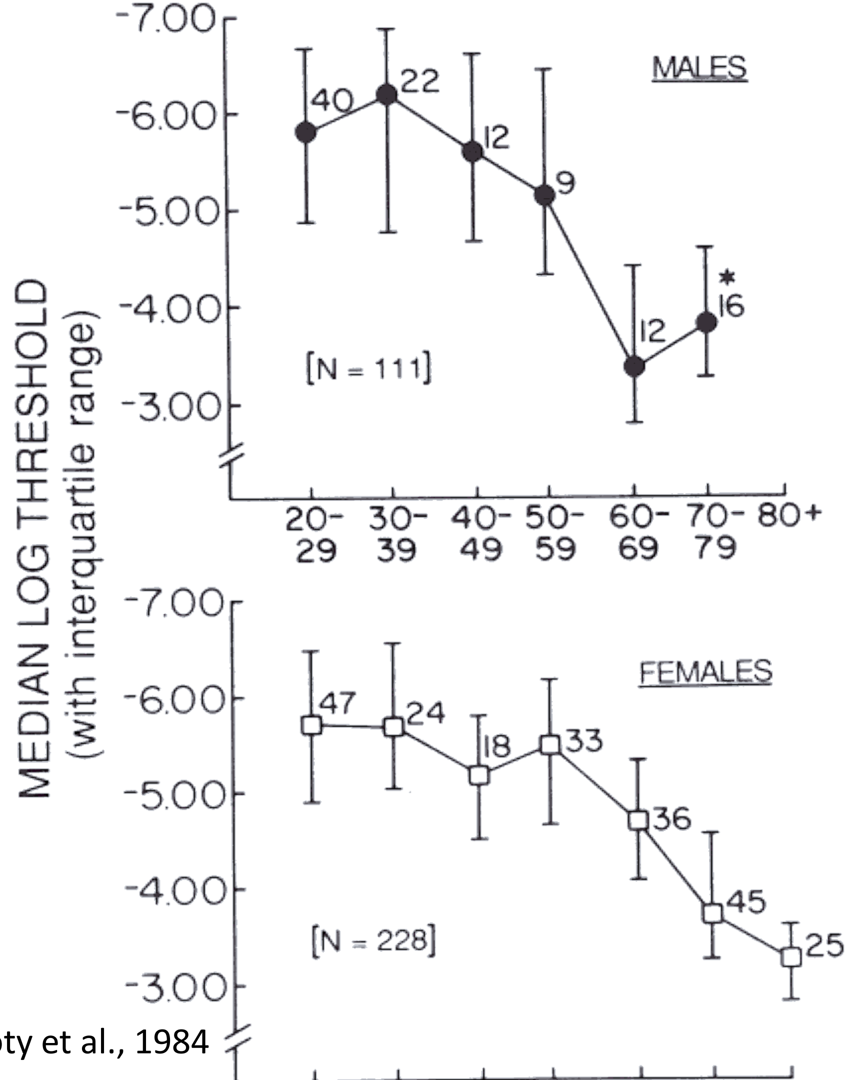
Orthonasal **Retronasal**

The nose and the mouth are connected

- Directly linked to emotional and memory centers in the brain

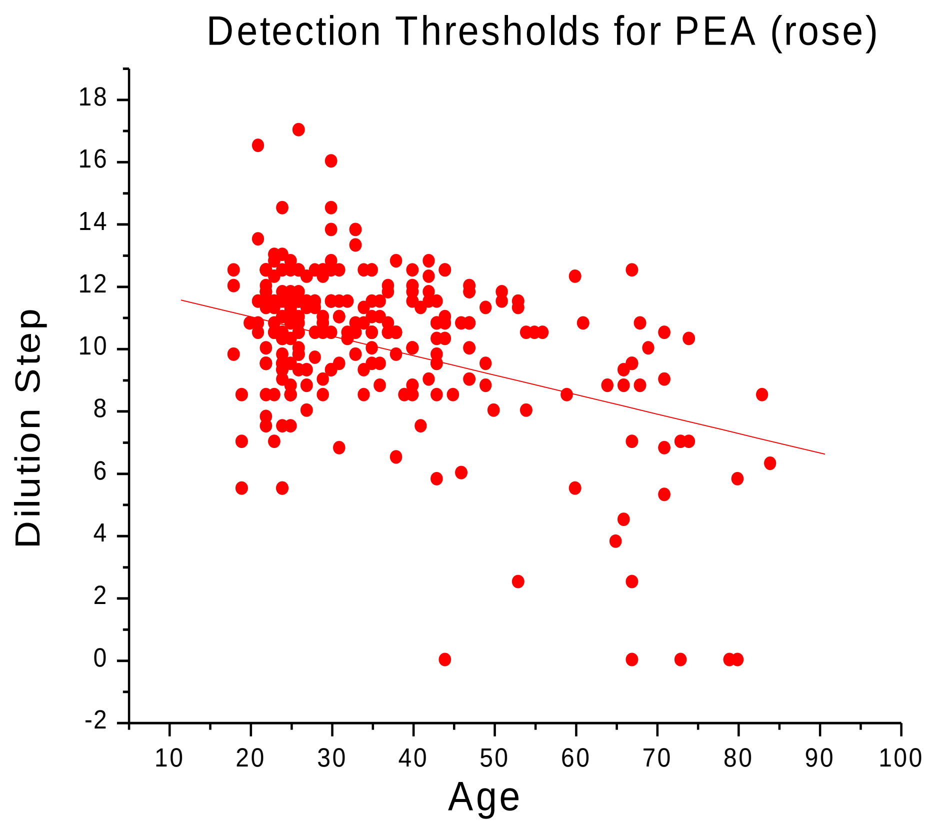
Ability to detect odors declines

By the time we reach 60, odor sensitivity has decreased about **2.5** - **3** orders of magnitude.



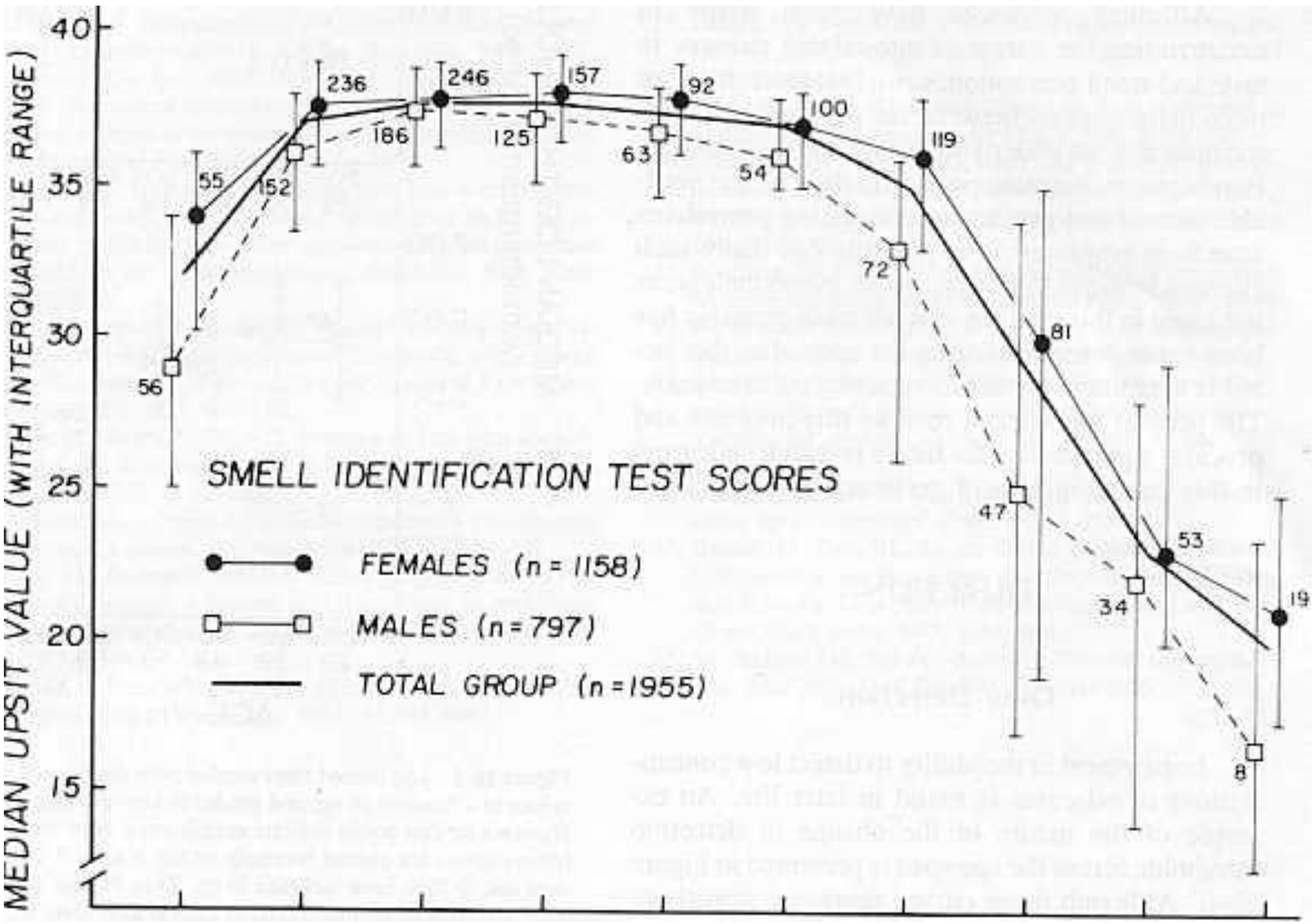
Doty et al., 1984

Considerable variation is evident



Rawson et al., 2012

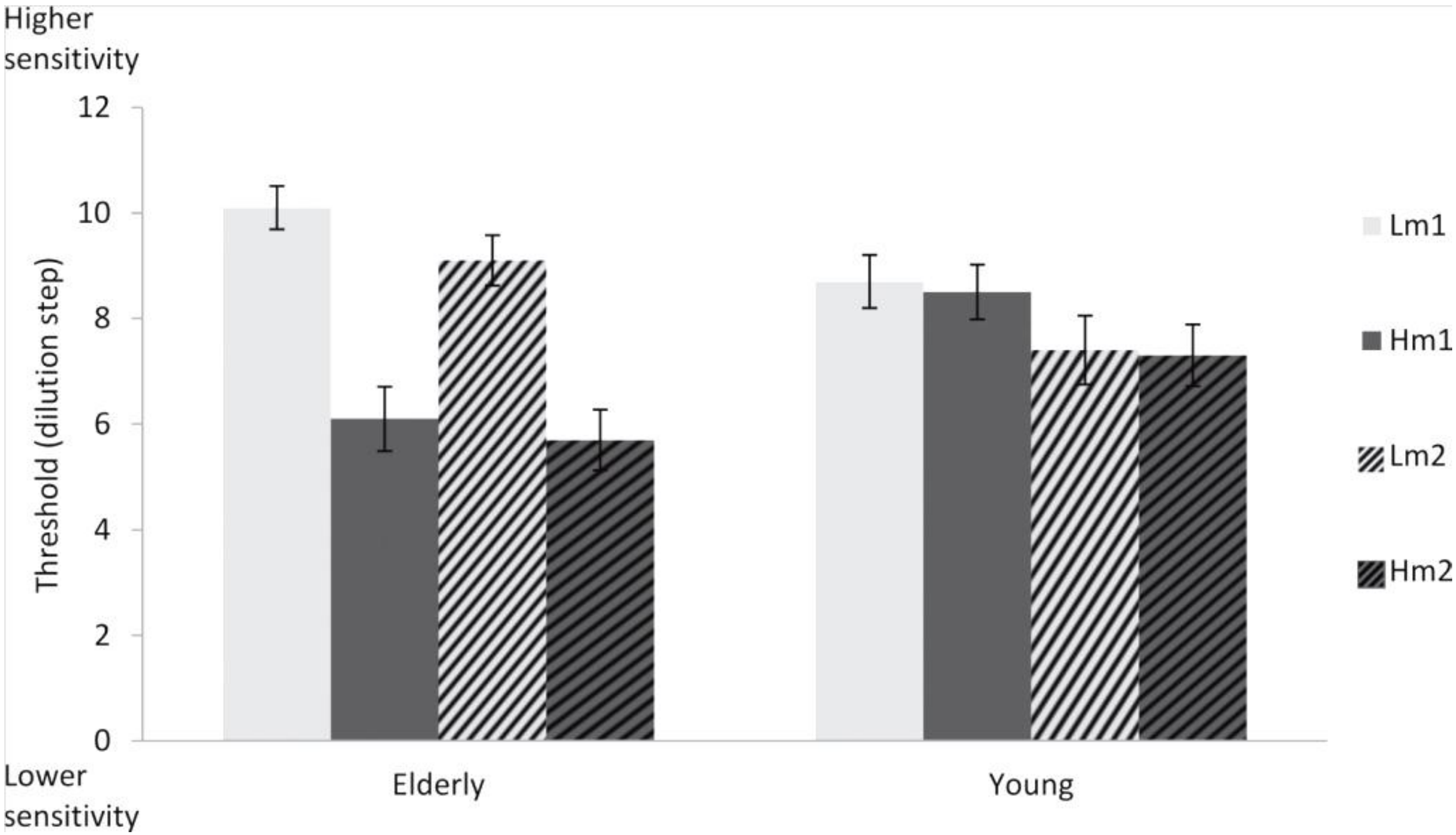
Olfactory identification ability declines



Doty et al., 1984

Heterogeneous loss

Sensitivity to larger (high molecular weight) odors was reduced to a larger degree than sensitivity to smaller (low molecular weight odors) (Sinding et al., 2014)



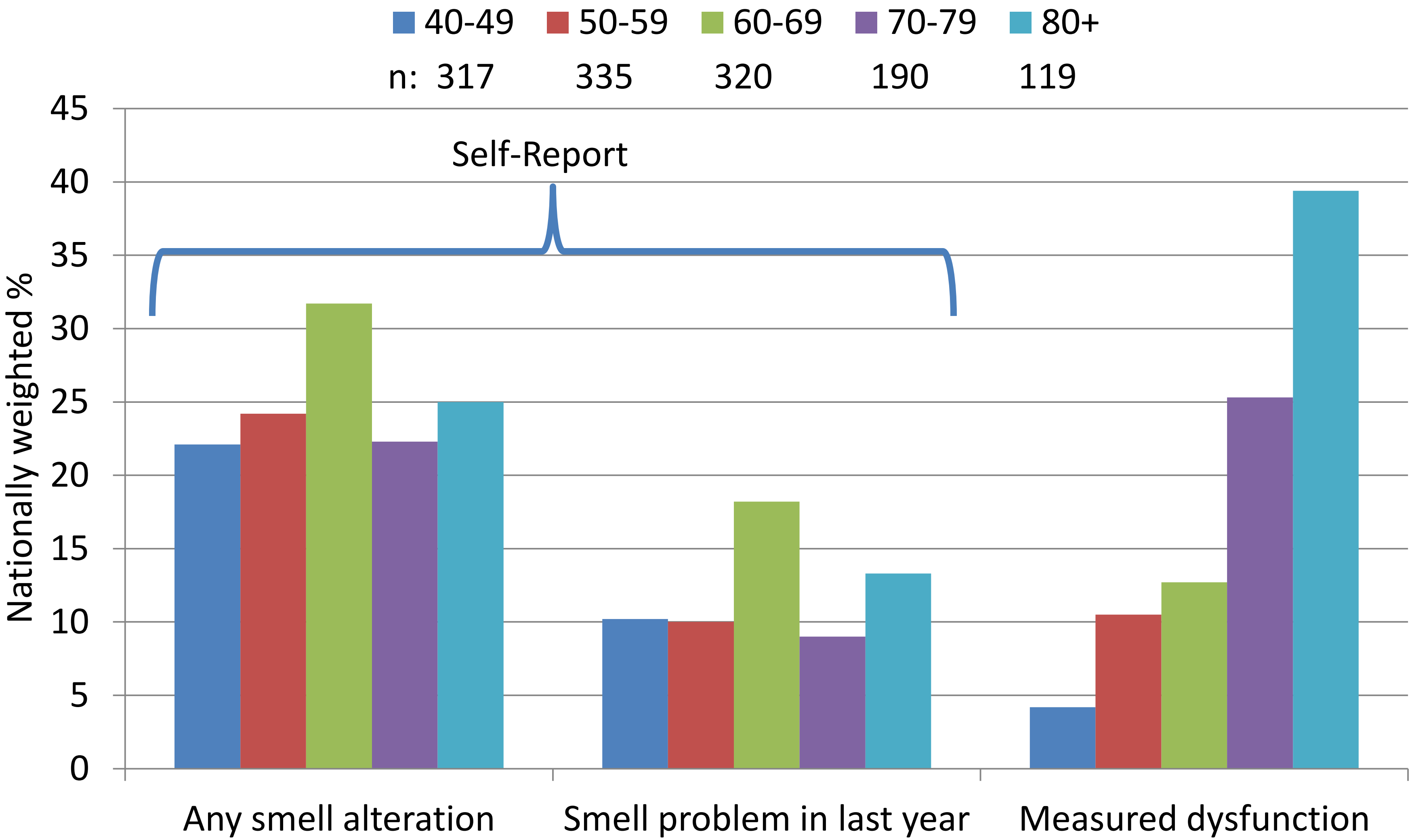
Larger odors are detected more anteriorly than smaller odors. (Scott et al., 2014)
The anterior epithelium is more susceptible to damage (Loo et al., 1996)

NHANES 2011-2014

- Olfactory data from 1281 participants $\geq$ 40 yrs in 2012
- 8-item, forced-choice, odor identification task
- Self-reported smell alterations during past year relative to age 25
- History of sinonasal problems, xerostomia, dental extractions, head/facial trauma, chemosensory-related treatment or changes in quality of life

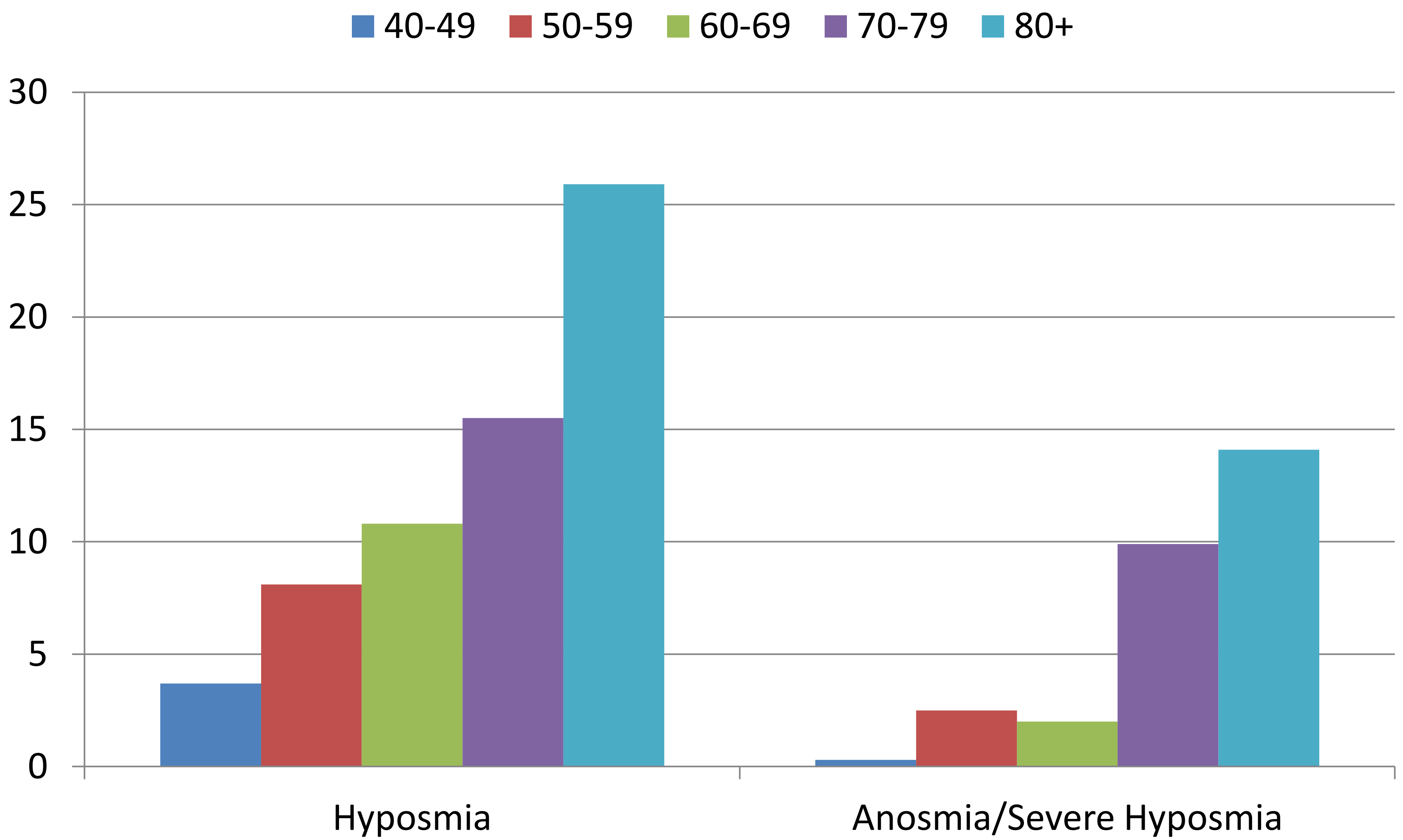
Hoffman et al., Rev Endocr Metab Disord, 2016

2012 NHANES Olfactory Results



Hoffman et al., Rev Endocr Metab Disord, 2016

Prevalence of measured smell dysfunction NHANES 2012 (n = 1281)



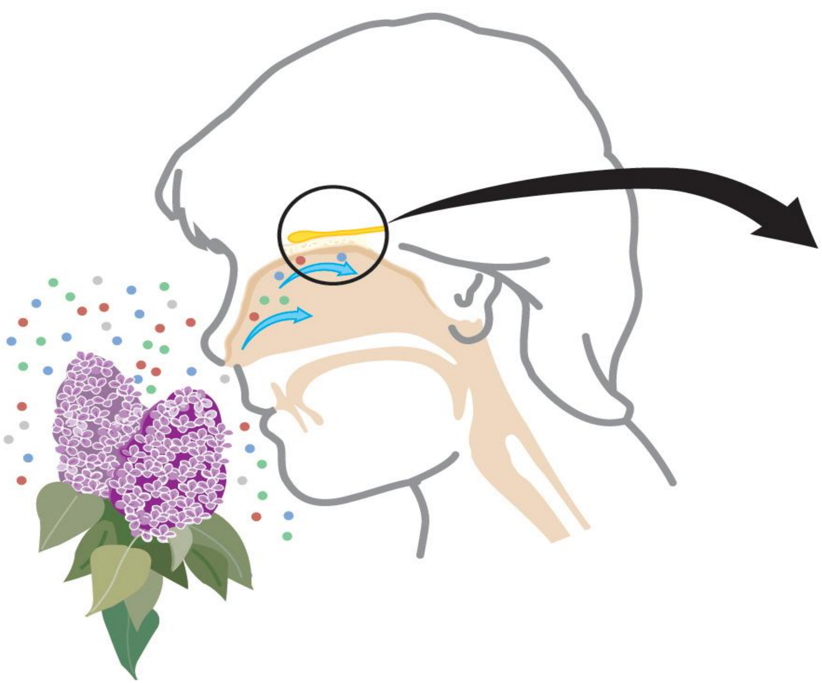
Hoffman et al., Rev Endocr Metab Disord, 2016

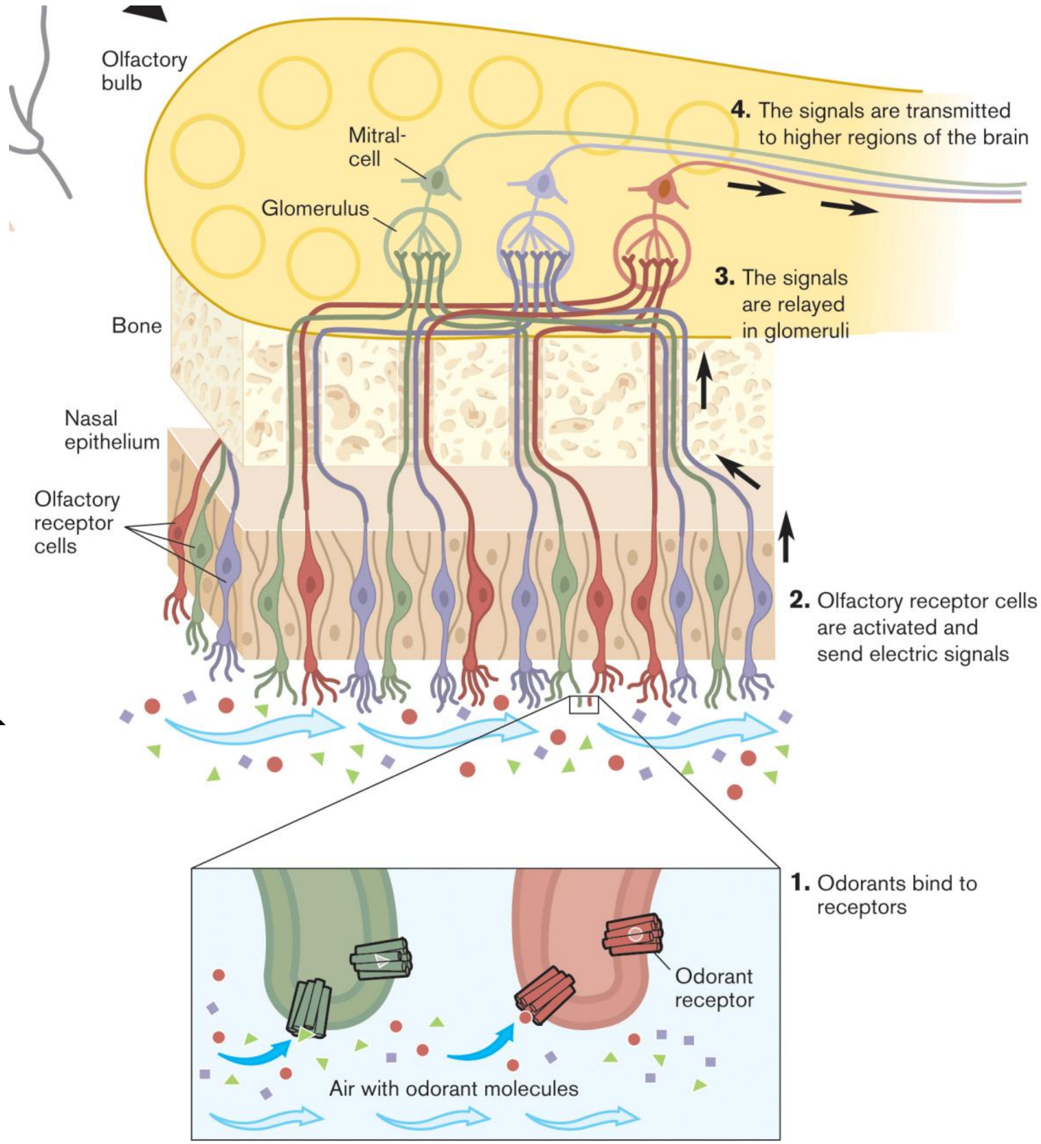
WHY?

Significant factors – NHANES 2012

- Subjects with a measured smell dysfunction were more likely:
  - Older
  - Male
  - Mexican-American
  - Lower Income-to-poverty ratio
  - Poorer general health
  - Not regular exercisers (mod-vigorous)
  - Heavy drinkers (4-5+/day)
  - Have had 2+ sinus infections
  - Have had wisdom teeth or tonsils removed or had ear tubes

Chemical Sense: Smell

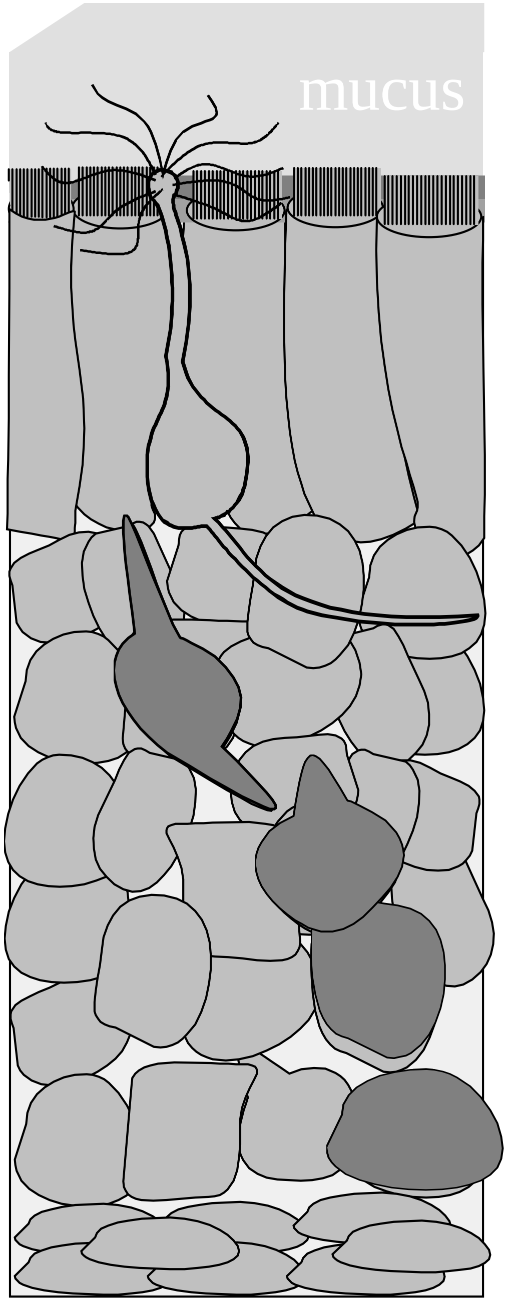




- Olfactory mucus protects & transports
- ~400 functional receptor types in the nose
- Substantial individual differences
- Olfactory epithelium can regenerate

Diagrams Courtesy of J. Mainland

Olfactory cells are replaced



6. Supporting cells

Odor Degradation

Ion balance

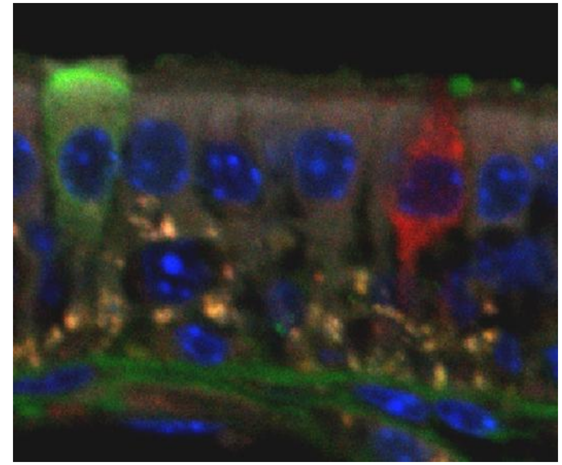
4. Immature ORN

3. Precursor

2. Progenitor

1. Globose Basal Cell

0. Horizontal Basal Cell



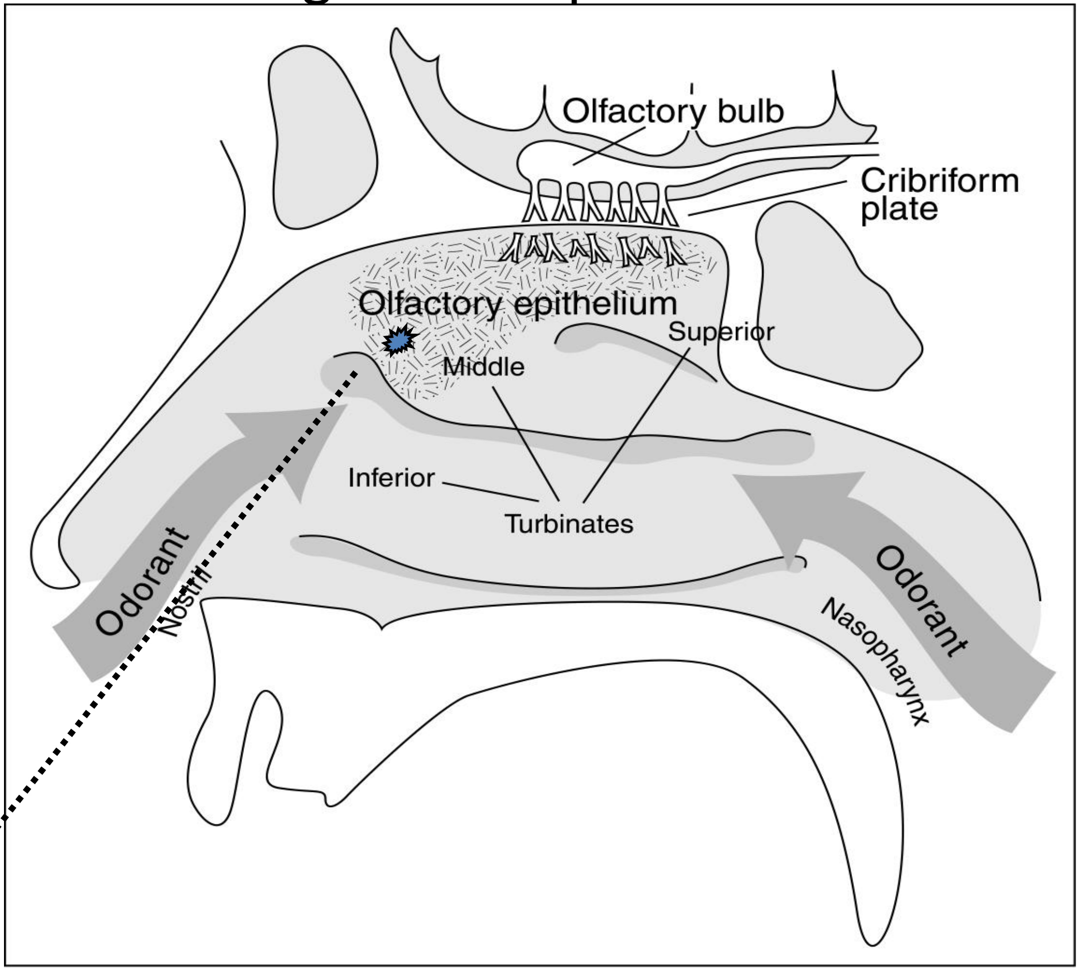
Mature receptor neurons are replaced from precursors within the layered epithelium.

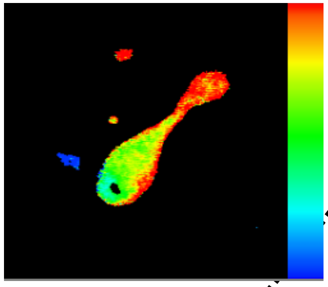
A variety of growth factors, including retinoic acid, regulate this process and may prove useful in promoting recovery from olfactory loss. (Paschaki et al., 2013; Rawson & LaMantia, 2006; Yee & Rawson, 2000)

Repair & Regeneration

- Damage from infection, xenobiotics, inflammation throughout life.
- Olfactory neurons can be grown in vitro.
- Telomere shortening impairs regeneration from injury, not under homeostatic conditions (Watabe-Rudolph et al., 2011)
- Retinoic Acid promotes OSN differentiation during early development (Rawson & LaMantia 2007)
  - Faster recovery following nerve transection (Yee & Rawson, 2000)
- Activation prolongs lifespan of neurons
  - Olfactory training can improve sensitivity
    - Kim et al., 2015; Altundag et al. 2015; Mori et al. 2015

Are there age-related changes in the presence or function of OSNs?



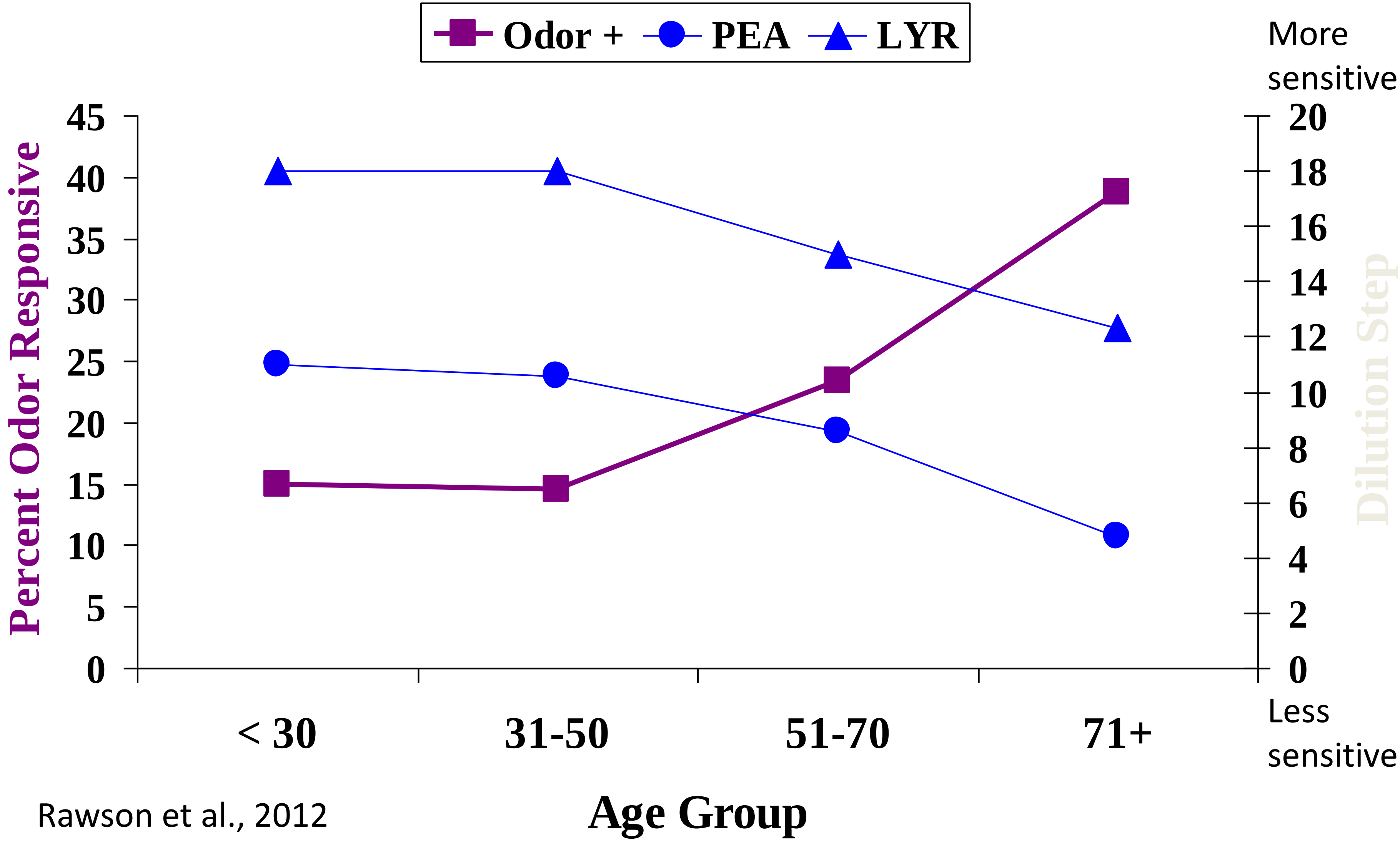


Biopsy

Nearly over 600 neurons from 440 subjects 18 - 88yrs old
Tested individual olfactory neurons to odor stimuli

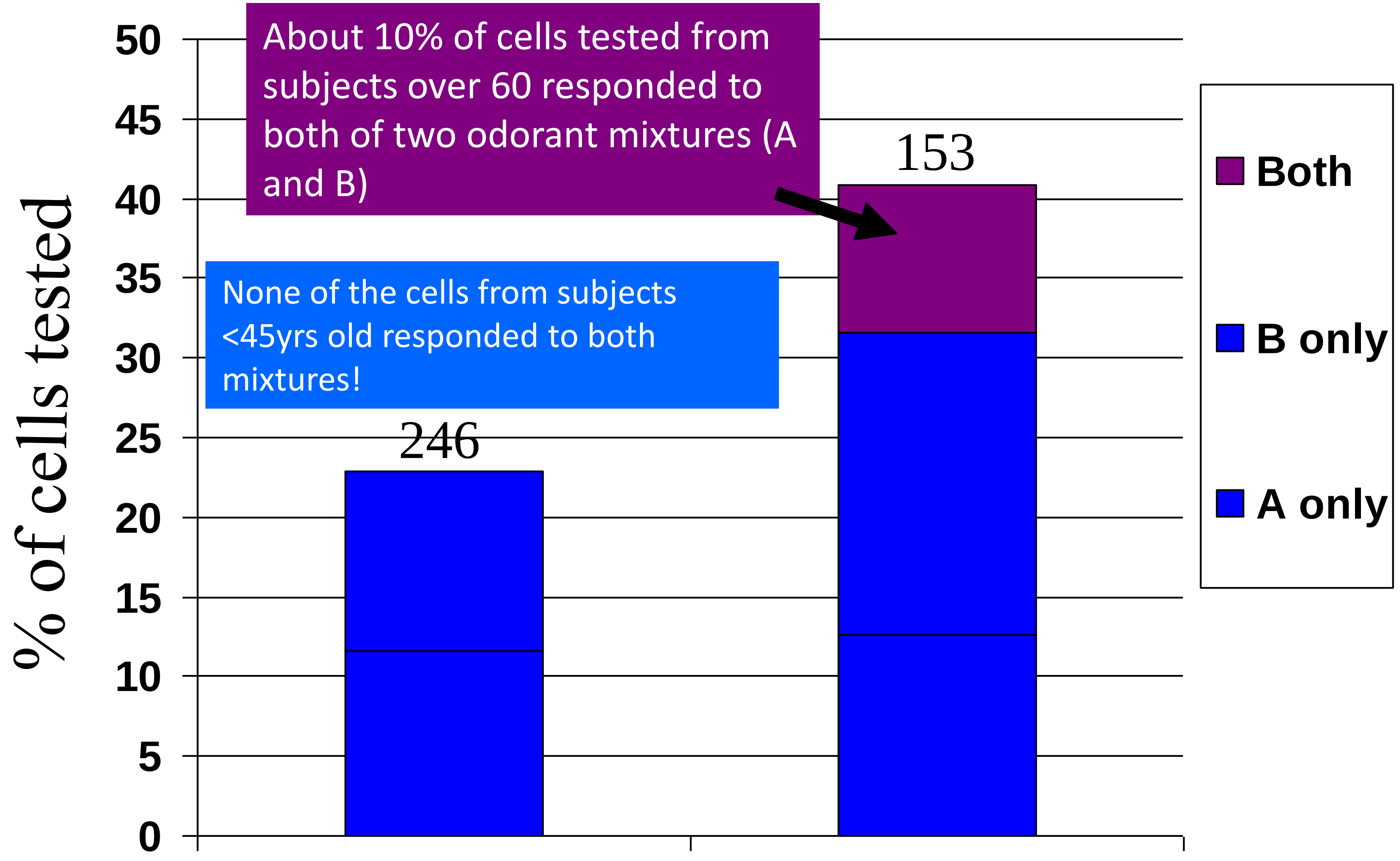
Rawson et al., 2012

As sensitivity decreases, the frequency of responsive OSNs increased.



Rawson et al., 2012

This increase is due in part to a loss of selectivity



Rawson et al., 2012

Loss of olfaction with aging

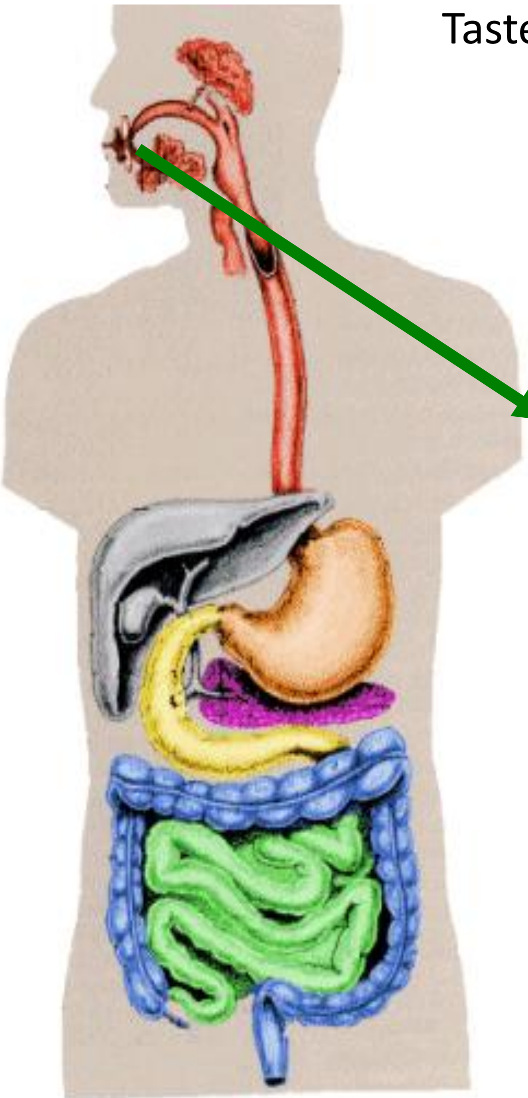
- Sensitivity to odors declines, although this change is gradual and not universal
  - Patchy epithelium
  - Changes in sniffing, mucus secretion
- Poorer ability to identify discriminate odors
  - More broadly tuned receptor cells
  - Changes in the CNS
- Faster adaptation, slower resensitization
- Self-report poor indicator of measured function
  - Changes across decade

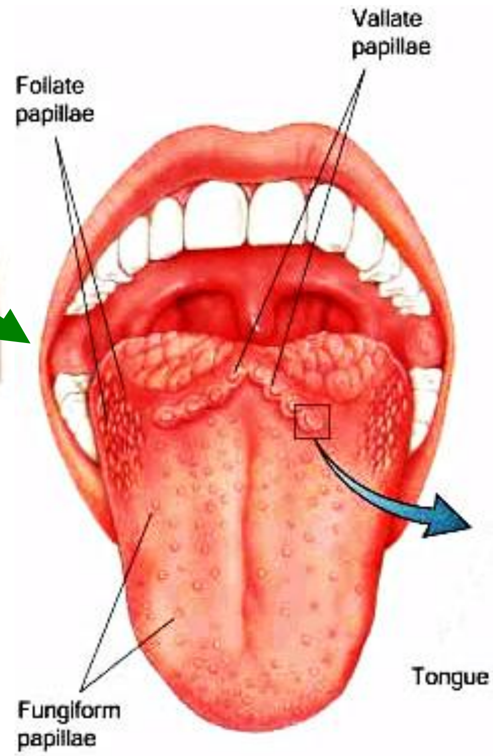
Chemical Sense: Taste

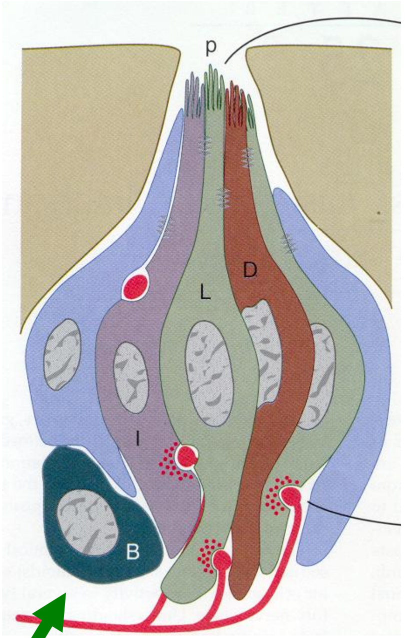
- Oral taste receptors
  - Sweet, sour, salty, bitter, umami, others?
- Function: nutrient evaluation
- Extra-oral "taste receptors"
  - Gut, pancreas, lungs, airways, testis, brain, others?

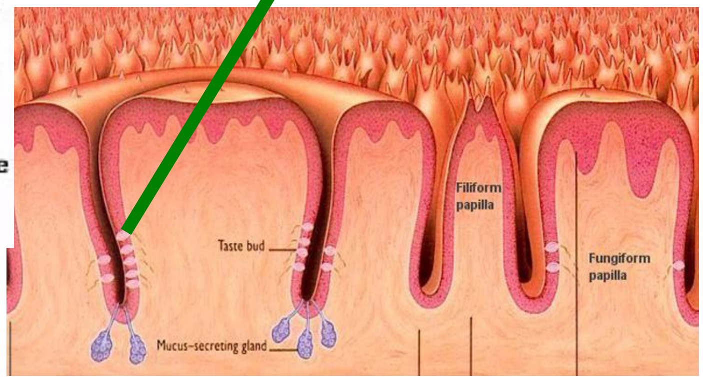
The Tongue's Taste Cells are the Initial Chemosensors of the Alimentary Tract

Taste stimuli must dissolve in saliva





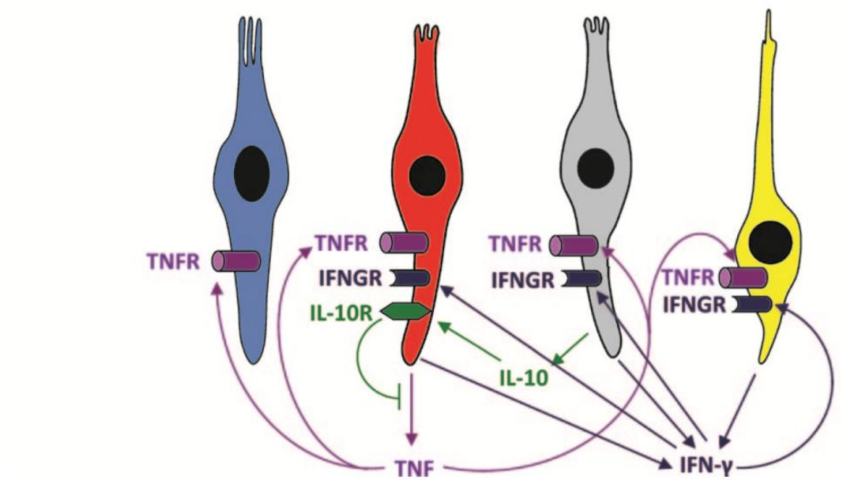




Diagrams courtesy of R. Margolskee

Regeneration & Repair

- Mature taste cells replaced from basal cells
- Taste cells can be generated in culture
- BDNF required for taste bud innervation
- Immune modulators released by taste cells
- Inflammation impairs taste cell generation

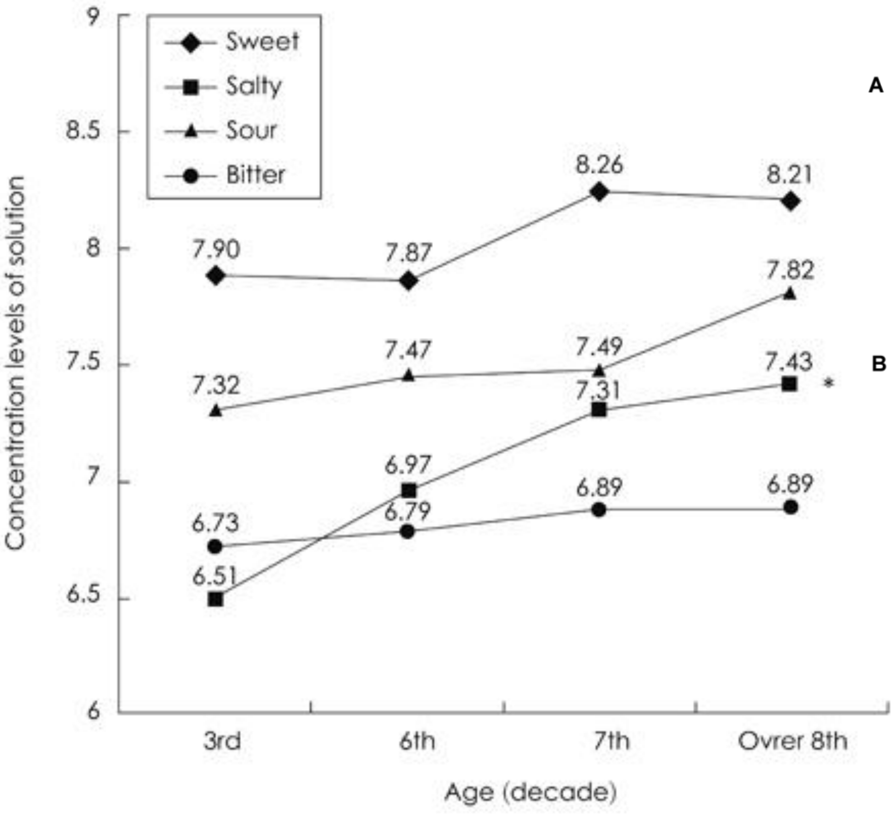


Cell Type	Type I	Type II		Type III
	Salty?	Sweet/ Umami	Bitter	Sour
TNF	-	+	-	-
TNFR	+	+	+	+
IFN-γ	nd	+*		+
IFNGR	nd	+*		+
IL-10	-	-	+	-
IL-10R	-	+	-	-

Maintenance of taste cells is sensitive to nerve damage, mitotic inhibitors, inflammation
Rawson et al., Yee et al., 2013; Takeda et al., 2013; Nguyen et al., 2012; Feng et al., 2013

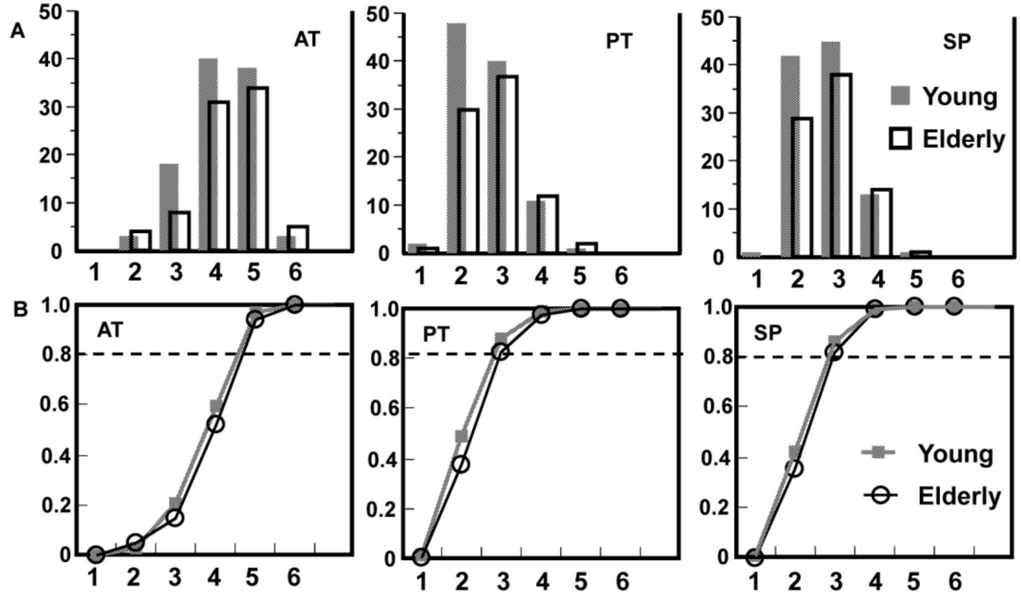
Some detection thresholds shift

Korean study (Lee et al., 2013)



Sweet, Salty more affected with age than Bitter, Sour

MSG Detection: Satoh-Kuriwada et al., 2014



Y = 18-25 yrs; Elderly = 65-89 yrs

Umami detection maintained

Taste changes with age

- Sensitivity:
  - Some change in all qualities, especially in 80+
  - Differences among specific taste stimuli
    - Sour, Bitter
- Discrimination, Identification and Suprathreshold Intensity reduced
- Most with taste loss also have olfactory loss

Anatomical Changes?

DENSITY

Shimizu 1997: 0 – 97 yrs, n = 241

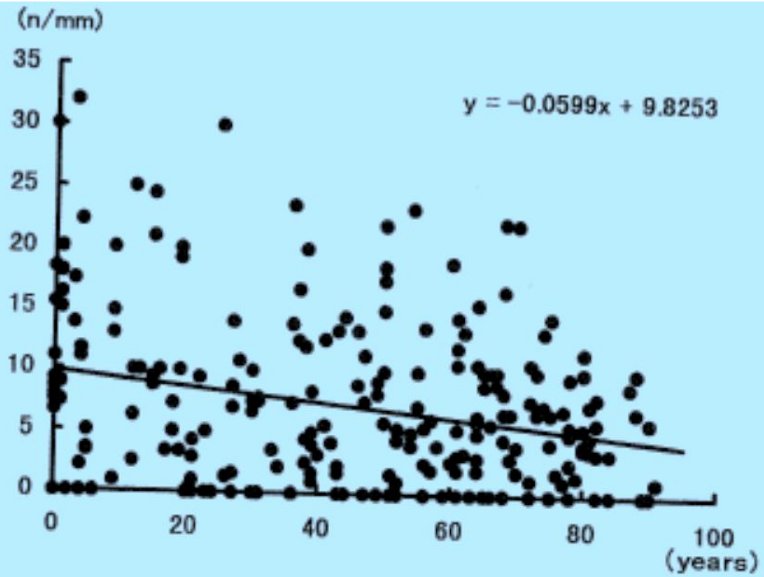


Fig. 3-1: Scatter diagram for age-related changes of taste bud density.

NUMBER

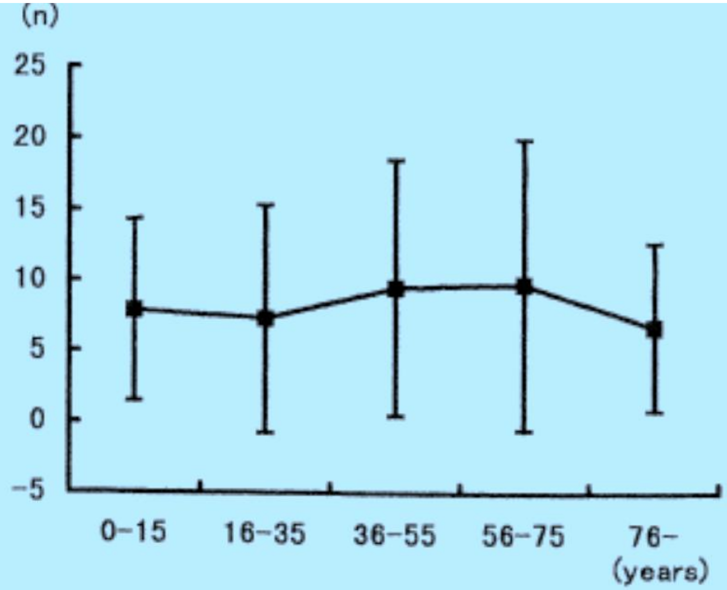
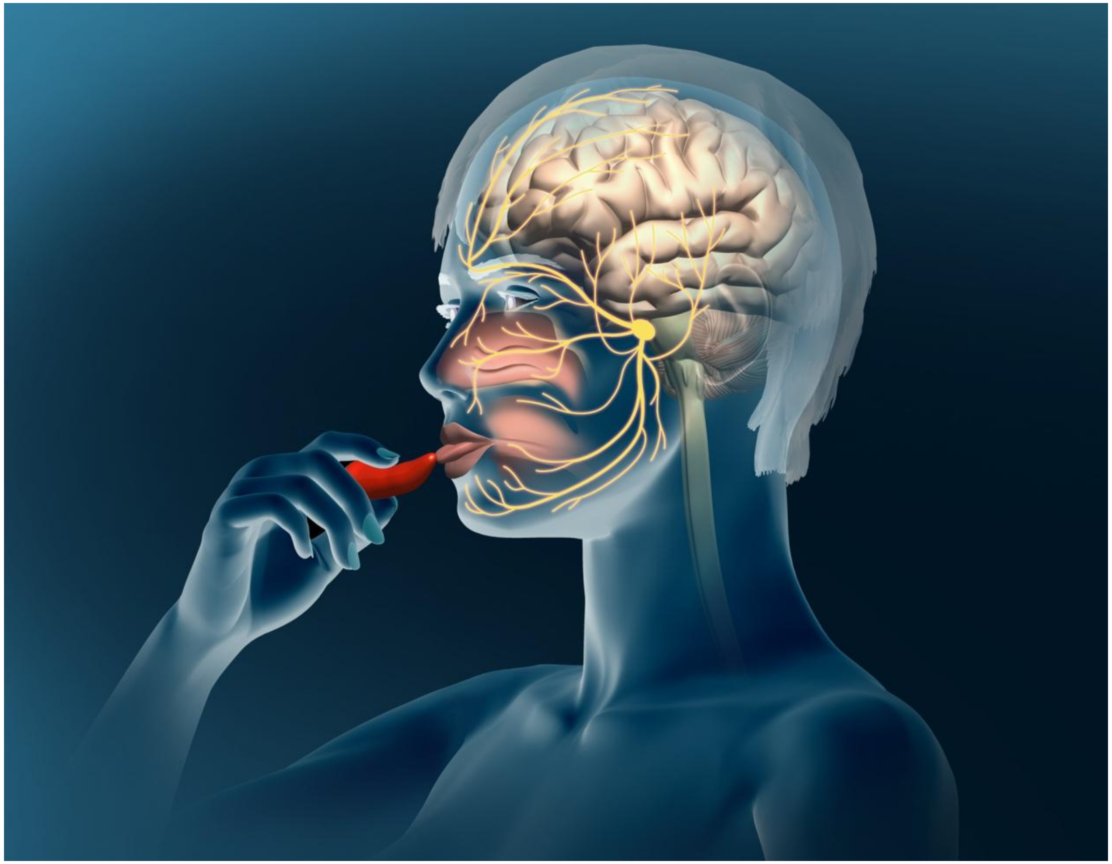


Fig. 3-2A: Relationship between age group and total number of taste buds.

- Taste Papillae size was similar
- Taste bud size was larger with increasing age!
- Fewer innervated papillae (Pavlidis, 2013)

Chemesthesis

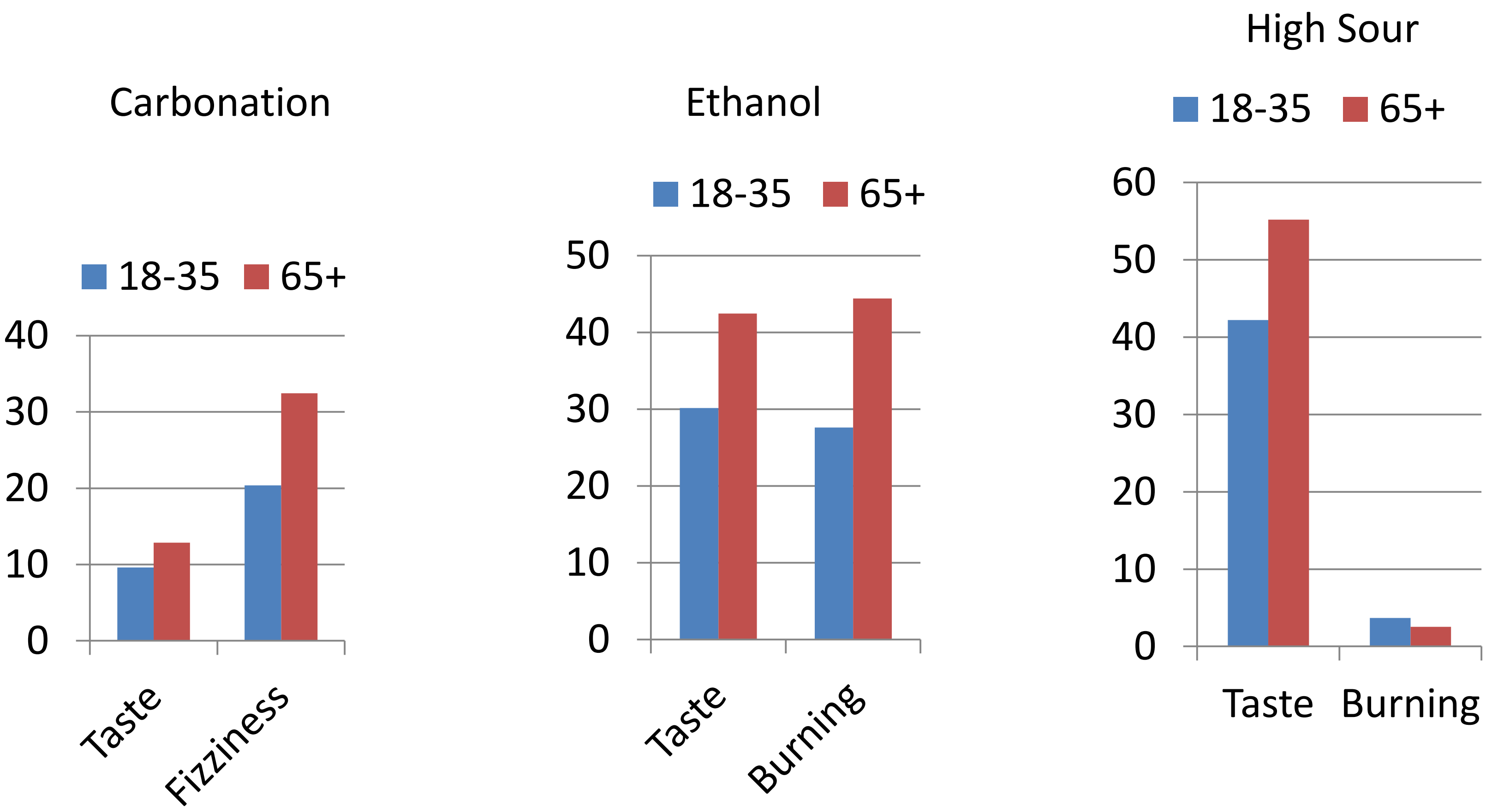


Cooling
Warmth
Itch
Stinging
Burning
Tingling

Warns us of danger, but also adds a sensory dimension to food which can be pleasurable

Oral chemesthetic stimuli rated as more intense by older subjects

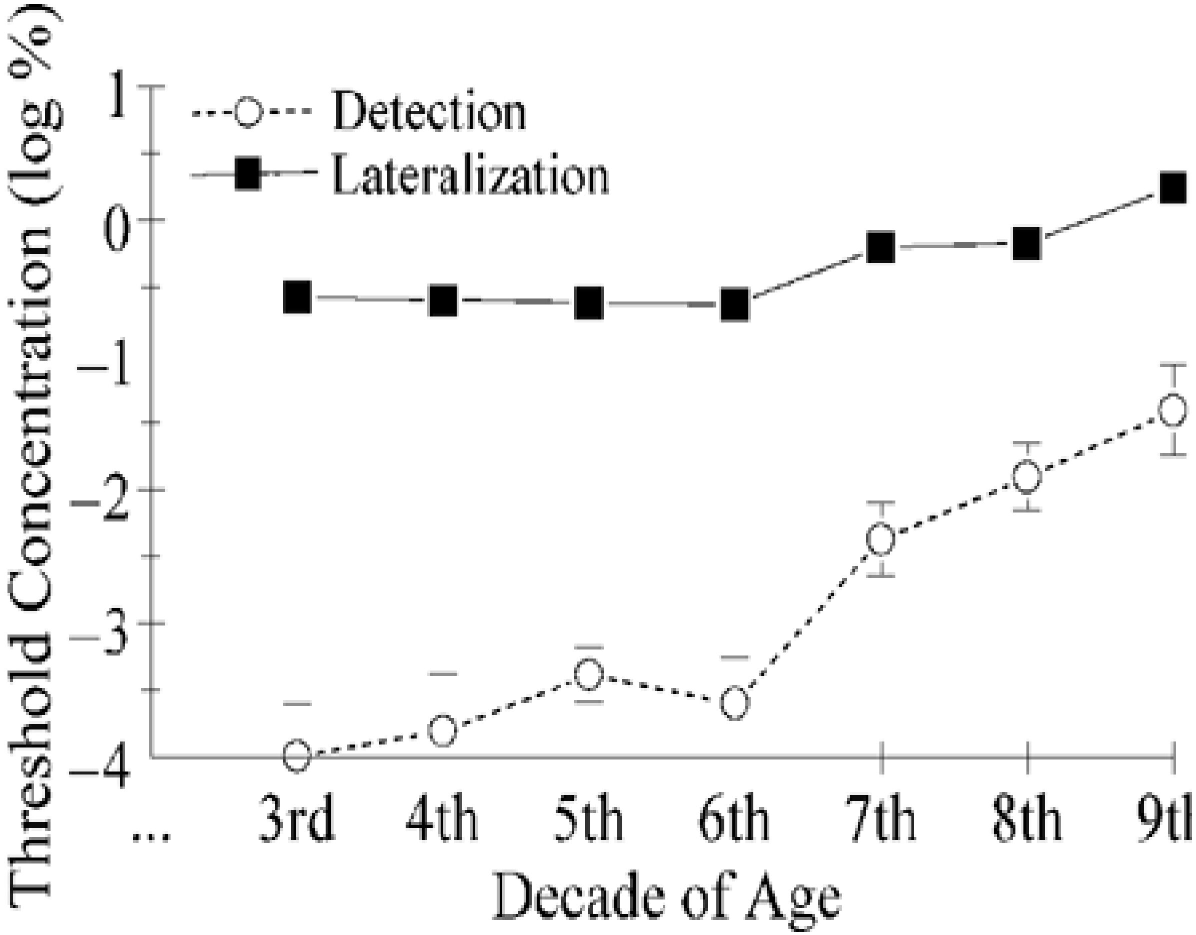
Ratings (0 – 100 on gLMS)



Pelletier & Steele, 2014

Nasal chemesthesis

Stimuli acting on the trigeminal nerve can be localized (L/R side)
Stimuli acting solely on the olfactory system cannot
The odor quality is perceived at lower concentrations than the irritation

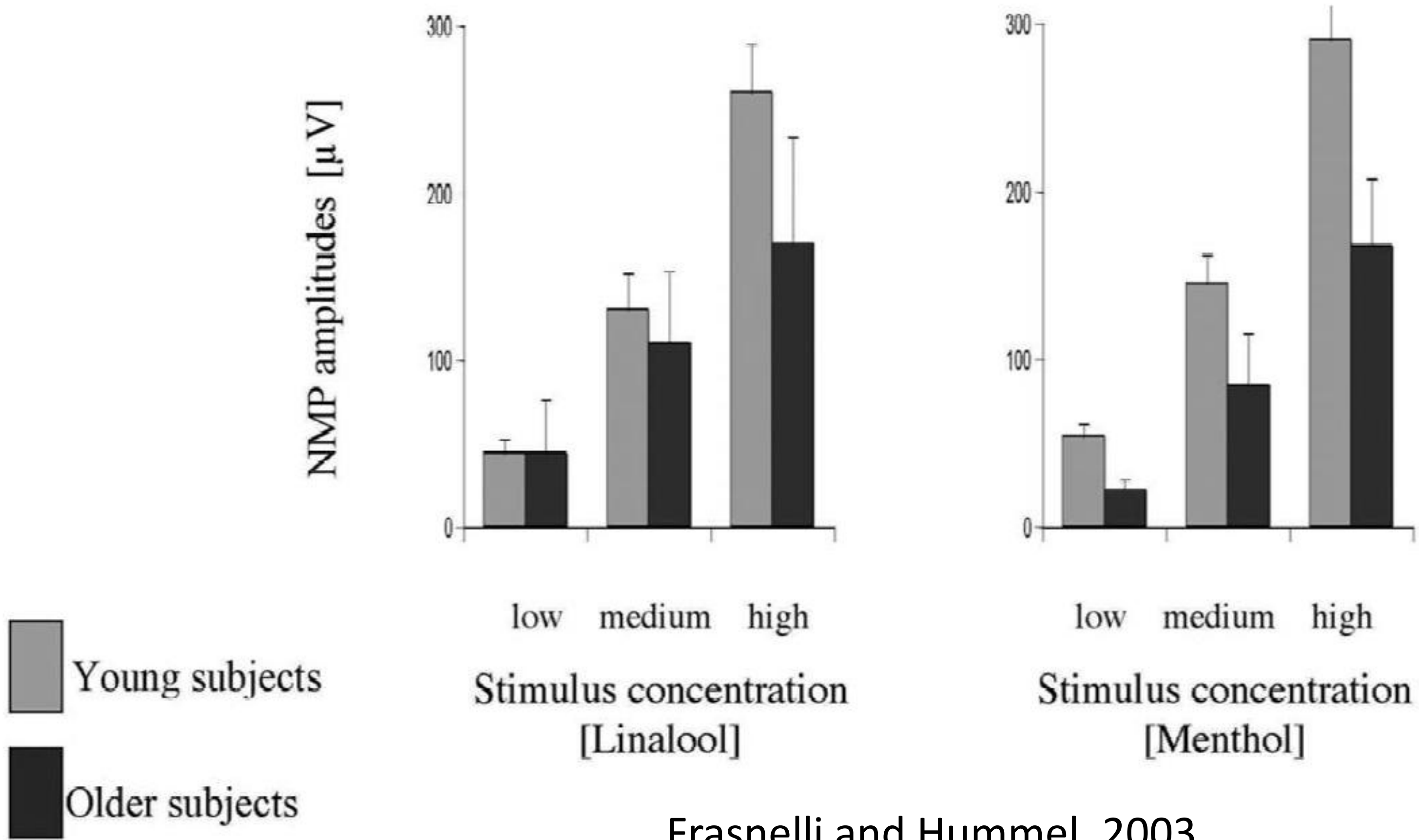


Older subjects require higher concentrations for lateralization as well as odor detection of chemesthetic stimuli (butanol)

Wysocki et al, 2003

Neural response is reduced

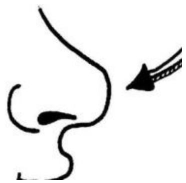
Negative mucosal potentials reflect activation of the nasal sensory nerves: Responses were lower in older subjects, particularly at higher concentrations.



Frasnelli and Hummel, 2003

Similar results obtained with other neurophysiological measures

Food Enjoyment is Multisensory



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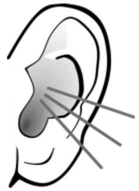

- Crunch
- Slurp
- Snap
- Crackle

Sensitivity across all of these modalities is impaired to varying degrees by aging and age-related factors such as medication use, dental status, hydration state

Sensory loss is a significant risk factor for poor diet and increased mortality

Thank You!

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