Olfaction 2016

Anosmia Stinks

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Olfaction 2016

- Considerable new work over last year or two- (since Dr. Gold's presentation)

Olfaction 2016

- Taste- involves Glossopharyngeal, Facial and Vagal nerves- recognizes basic tastes- sweet sour, salty, bittter and umami (glutamate)
- Olfactory Nerve- wide range of odorants- odor molecules pass to olfactory epithelim
- Trigeminal Nerve- Sharpness of horseradish, cooling of menthol

Olfaction 2016

- Olfactory receptor neurons in olfactory epithelium are exposed
- Olfactory cells regenerate continuously, but diminishes with age (good news)
- Odor molecule must diffuse through the mucous to get to mucous membranes

Olfactory Disturbances

- Affect up to 20% of population

- Negative impact on quality of life-
  - Enjoyment of food
  - Detection of dangerous odors/spoiled food
  - Associated with mild-severe depression
  - Alterations in food intake

Olfaction 2016

- Smell becomes worse the more medications are taken
- Life expectancy negatively associated with lowered olfactory abilities
- Women superior to men in olfactory function

Causes of Loss of Olfaction

- Common
  - Nasal and sinus Disease-obstructive/inflammatory
  - Post Viral
  - Head Trauma
  - Smoking
  - Neurodegenerative Disease
  - Age

Less common Causes

- Medications
- Cocaine
- Toxic exposure- benzene, butyl acetate.chlroine, formaldehyde, ethyl acetate, paint solvents, others
- Industrial exposure-heavy metals,
- Nutritonal Factors- Vitamin A, B6, B12, trace metal deficiencies

Uncommon causes

- Neoplasia
- Radiation
- Psychiatric
- Endocrine- cushings, diabetes, hypothryoidism, Kallman's syndrome
- Olfactory aura in seizures/migraines
- CVA,
- Autoimmune- Sjogrens, Lupus

Medications

- Just about every medication from antibiotics to statins has been indicated

Zinc

- Zinc gluconate applied intranasally caused anosmia in rats

(food finding time)

Zicam

Olfaction 2016 Parksinon’s

- Smell disorder in 95 per cent
- Olfactory distorder may precede motor symptoms by 4-6 years on average

Olfaction/Alzheimer's

- Study: Patients with mild cognitive deficits
- Those with lower olfactory scores were more likely to develop Alzheimer's at 2 year follow up

Olfaction/Alzheimer's

- 308 community patients in Australia 2013- high risk normals 46-86 yoa
- Follow up at 3 years
- Those with diminished olfaction were significantly more likely to have cognitive decline at 3 years.
- ?use as predictor of cognitive decline?

Newer Work

Exercise

- Schubert et al 10/2013
- 10 year follow up of normals- cumulative incidence of anosmia 27.6%
- (worse if older, male)
- 40% rate if exercised once a week

  (to work up sweat)
- ? Exercised because healthier???

Tumor Necrosis Factor- alpha

- TNF alpha- inflammatory cytokine- causes loss of smell in rats
- Treatment with oral steroids prevented this loss

- ? Use of prednisone in loss of smell

Interleukin 6 in Hyposmia

- IL-6 is an inflammatory mediator- pro inflammatory cytokine
- Henkin et al 2013

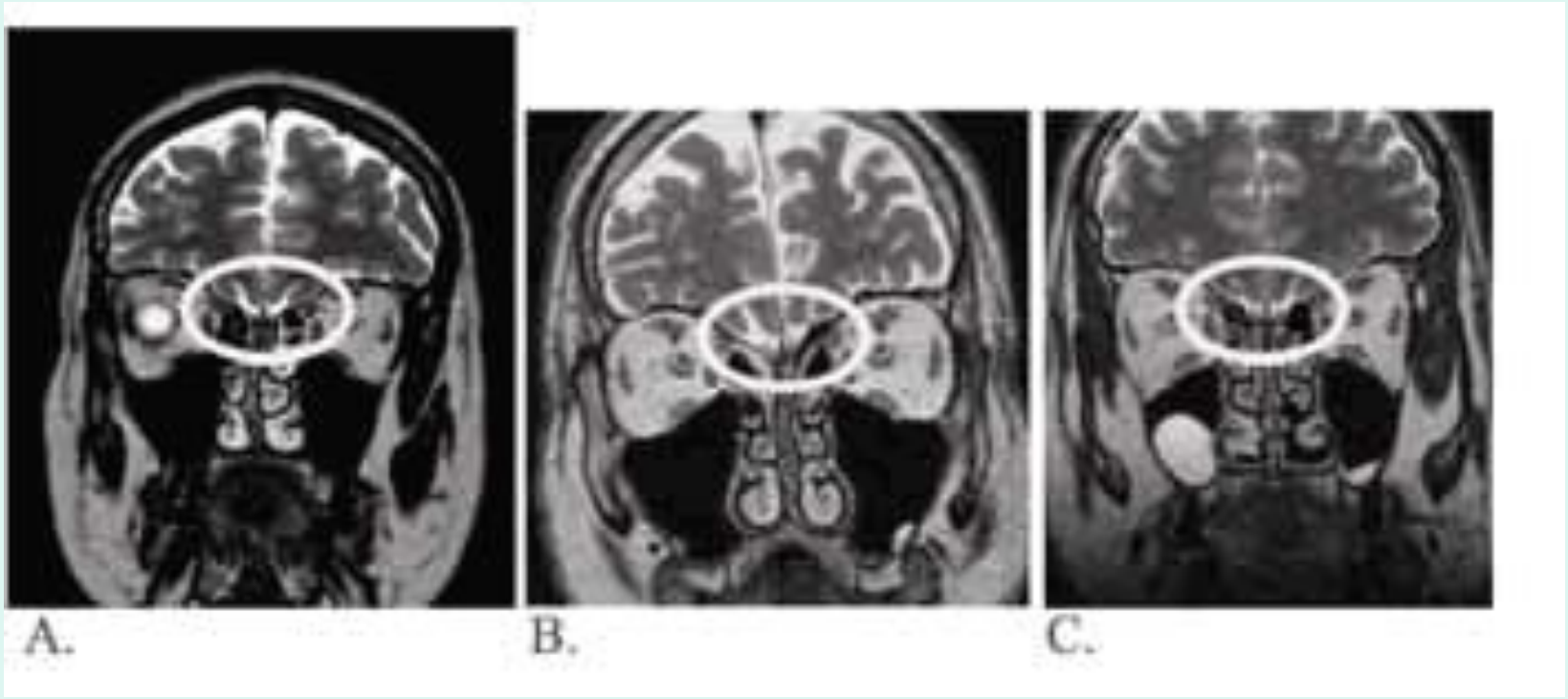
  IL-6 is increased in nasal mucous of patients with hyposmia compared to controls

Highest in pts with burning mouth syndrome, post viral, head trauma and lowest with allergic rhinitis

Measurement of Olfactory Bulb (OB)

- Correlates to loss of smell
- Diminishes in size with loss of function
- (laryngectomy, polyps)
- Predictor of return of sense of smell

Coronal T2 MRI Olfactory Bulb- normals



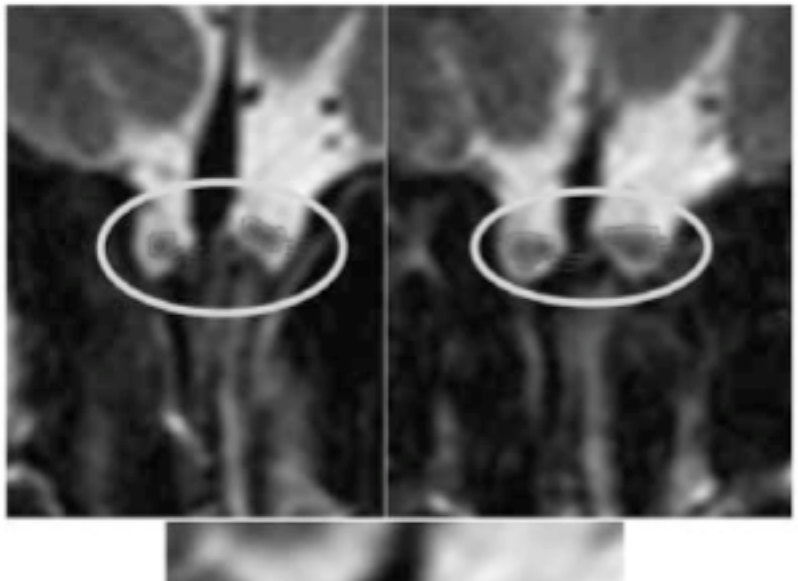
Olfactory Bulb

anosmia_ct (page 2 of 7)

why processes of cell death and
he OB, resulting in continual
onnections. It has been shown
eurogenic system is of primary
euroblasts migrate to the OB via
, starting at the subventricular

ry tract, which runs at the skull
fferent projections; the internal,
s the connections of which ter-
y cortex. Primary olfactory cor-
ory nucleus (in humans integrat-
, the piriform cortex, the peri-
la, the entorhinal cortex and its
viewed as a center of great com-
e connections at several levels
uit of informations as well as a

Figure 1. Coronal and sagittal T2 weighted sequence, reconstruction from horizontal plane OB volume (arrow) and olfactory tract.



OB size and return of olfcation

- Rombaux et al 2012
- 60 patients with acquired hyposmia

  28 post infectious 32 post trauma

Sniffin test at first eval and 15 months

36% post infectious improved-

25% post trauma improved

OB size and return of Olfaction

- NO patients with OB <40 mm3 had return of function
- Initial measurement of OB is significant prognosticator of return of smell

Effects of Nasal Polyps on OB

Herzallah et al 2013

11 pts with polyps mean 10.14 mm3

11 pts w/o polyps mean 47.66 mm3

Olfactory bulb volume decreased in pts with nasal polyps

May help predict which patients will have improved sense of smell post FESS

OB and laryngectomy

- Significant decrease in average volume of OB at 6 months-

- 64.2 mm3 to 47.1mm3

OB and stimulation

- OB seems to diminish in size with lack of olfactory stimulation
- (nasal polyps, laryngectomy)

- Treat obstruction more aggressively?

Prognosis after Loss of Smell

- Women and younger> males and older
- Post infectious > post traumatic
  - Still about 1/3
  - ?Duration of Disease

Is Treatment Possible?

- Costanzo et al 2011
- Sensory neurons in the olfactory epithelium showed to undergo continuous regeneration, grow new axons and reestablish connections with the olfactory bulb through life

Neural Regeneration

- Basic fibroblast growth factor applied to nasal epithelium improved neural anosmia in rats (CK?)

Effect of FESS on Smell

- Most studies show that this is difficult to predict
- Patients with nasal polyposis tend to have better chance of improvement

Olfaction and FESS

- 50-83 % improvement in Olfaction with FESS- greater in those with polyps and swelling in olfactory groove-
- 45-50% improvement in revision surgery at 16 months
- One study showed no improvement post FESS- and most patients remain severely hyposmic

Nasal Surgery and Olfaction

- Schreiver et al 2013
- Nasal polyps- 32 % improved sense of smell at 12 months
- No significant improvement for sinus surgery (17%) or septal surgery (0%) without polyps at 12 months

Impaired Sense of Smell- nasal surgery

- Briner 2004
- 84% of patients with pre-operative losses (16/19) were aware
- 4/184 nasal/sinus patients with new onset of impaired olfaction post surgery

- ? Smell test pre-op?
- ? MRI of OB to help predict improvement?

MRI Screening for Anosmia

- Northwestern University
- 122 patients with anosmia
  - Normal MRI 44.3 %
  - Dysosmia related findings 25.4% most common frontoethmoiditis
  - Incidental findings 40.2% -(eg small vessel disease 21.1%)
  - 9 patients with intracranial findings- 6 intracranial neoplasms (4.9%) including olfactory meningiomas

MRI Screening for Anosmia

- Cost $48,880 per intracranial neoplasm found
- Cost $146,600 per intracranial neoplasm found that was cause of anosmia
- Average malpractice settlements for missed diagnosis or delayed treatment for intracranial neoplasm 1997-2003 was between $600,000 and $6,000,000
- ????? Not sure that this makes sense but they felt one should therefore do MRI.. Did not compare to general well population..

Treatment

- Konstandinidis et al 2013
- 119 patients with new onset anosmia - post traumatic and post infectious
- 16 weeks of Olfactory Therapy

Olfactory Therapy

- Twice daily training with 4 odorants for 16 weeks
- Rose, eucalyptus, lemon, cloves

- Significant increase in olfaction in 2/3 post-infectious and 1/3 post-traumatic vs. controls

Olfactory Therapy

- “16 week short term exposure to specific odors may increase olfactory sensitivity in patients with post-infectious and post-traumatic olfactory dysfunction.”

Olfactory Therapy Parkinson's

Haehner et al

70 patients with PD - 35 Olfactory therapy

12 weeks

Significant increase in olfactory function with training, vs. no change in controls

Olfactory Training

- 18 weeks high training vs low training
- Post infectious

Duration	High training	Low
<24 months	26%	15%
<12 months	63%	19%

OT clearly helpful in those with post infectious loss of <12 months

Treatment of Loss of Smell

- Methylprednisone for 14 days

- 425 patients
- 26.6% improved- (36.7% if sinus disease)
- No controls

Medical Therapy

- Heilings 2009
- Both nasal and sytemic steroids showed improvement in smell function in patients with and without polyps- ? Obstruction to smell vs. inflammatory mediators. (IL6?)

Medical Therapy

- Post traumatic Anosmia- Prednisone
- 19/116 (16.4%) improved with steroids- (but no controls)

Treatment of Loss of Smell

- Reden 2012

- Vitamin A 10,000 units/day for 3 months

Post Traumatic and Post Viral

No significant difference in placebo vs. Vitamin A

Medical Therapy

- Henkin et al 2011
- 312 patients with hyposmia treated with oral theophylline
- > 50% with improved smell function
- All had low levels of cAMP and cGMP before teatment- responders tended to normalize

Medical Therapy

- Intranasal Theophylline

Decreased cAMP and cGMP in nasal mucous in patients with loss of smell and taste

Oral theophylline led to increases in >50% and correlated to increased smell acuity

Systemic side effects

Medical Therapy

- Intranasal theophylline (20ug in 0.4ml saline) once daily
- 10 patients: 3 atopy, 3 post viral
  2 post trauma 2 idiopathic
- 8/10 with signficant improvement at 1-4 weeks- rx stopped - 4 persisted at 10 weeks-

Intranasal Theophylline

- No blood levels of theophylline
- ? Diminishes allergic inflammation
- ? effect on OB
- ? Through blood brain barrier

Treatment for Loss of Smell

- Steroids- possibly more aggressive treatment of nasal obstruction to prevent OB changes
- Alpha Lipoic Acid- Himmel for post infectious
- Theophylline- intranasal (Pasteur)
- Smell Therapy
- ?
- Unproven: estrogens, zinc, minocycline, Vitamin A
- ? MRI for prognosis/ intracranial pathology

SO WHY THIS LECTURE?

- NYOG SINUS CENTER PROTOCOL

1. ANOSMIA