Olfaction 2016

Anosmia Stinks
Robert L Pincus MD
NY Sinus Center/ NYOG
Olfaction 2016

• Considerable new work over last year or two- (since Dr. Gold’s presentation)
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• Taste- involves Glossopharyngeal, Facial and Vagal nerves- recognizes basic tastes- sweet sour, salty, bitter and umami (glutamate)
• Olfactory Nerve- wide range of odorants- odor molecules pass to olfactory epithelium
• Trigeminal Nerve- Sharpness of horseradish, cooling of menthol
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- 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
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• 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, chlorine, formaldehyde, ethyl acetate, paint solvents, others
- Industrial exposure-heavy metals,
- Nutritional Factors- Vitamin A, B6, B12, trace metal deficiencies
Uncommon causes

- Neoplasia
- Radiation
- Psychiatric
- Endocrine- cushings, diabetes, hypothyroidism, 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 Parkinson’s

- Smell disorder in 95 per cent
- Olfactory disorder 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
  (laryngecctomy, polyps)
• Predictor of return of sense of smell
Coronal T2 MRI Olfactory Bulb - normals
Olfactory Bulb

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

- 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 prognosticato 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 mm$^3$ to 47.1 mm$^3$
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

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<thead>
<tr>
<th>Duration</th>
<th>High training %</th>
<th>Low training %</th>
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<tbody>
<tr>
<td>&lt;24 months</td>
<td>26%</td>
<td>15%</td>
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<tr>
<td>&lt;12 months</td>
<td>63%</td>
<td>19%</td>
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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 systemic 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 treatment - 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 significant 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