FLAVOUR KLINIKKEN

HOLSTEBRO - DENMARK

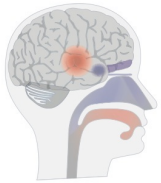
Sensoriske forandringer som senfølge hos COVID-19 patienter

Dansk Selskab for Klinisk Ernæring
Årsmøde 2021
07.05.2021

Alexander Fjældstad, læge, lektor
Flavour Klinikken, ØNH, HEV

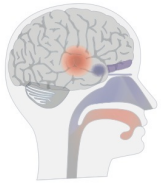
midt
Central Denmark Region

AARHUS UNIVERSITY



Relevans i DSKE-regi

- Sensoriske tab er relevante for ernæring og udarbejdelsen af ernæringsplaner for patienter
- God ernæringsvejledning kræver en individuel tilgang
- COVID-19 kan forårsage meget varierende sensoriske senfølger

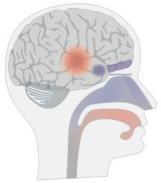


Sansetab

"Det er bedre at have elsket og mistet end slet ikke at have elsket.”*

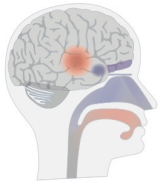
- **Alfred Lord Tennyson (1809-1892)**

*Det gælder dog ikke for patienter med fx lugtetab, der ofte mister kærligheden til mad og er meget mere påvirkede af sansetabet end patienter, der er født uden lugtesans



Er det overhovedet relevant?

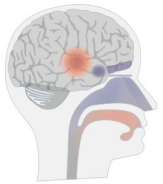
- Nedsat nydelse af mad (Største indvirkning på livskvalitet)
- Manglende registrering af fare (mad, røg etc.)
- Problemer med arbejde (sygeplejeske, pædagog, kok, politi etc.)
- Socialt hæmmende (kropslugte, partner, middage etc.)
- Øget risiko for angst og depression (lugtetab ←→ depression)
- Mest præcise symptom som markør for COVID-19
- Hyppigt vedvarende sansetab efter COVID-19



Hyppighed ved COVID-19

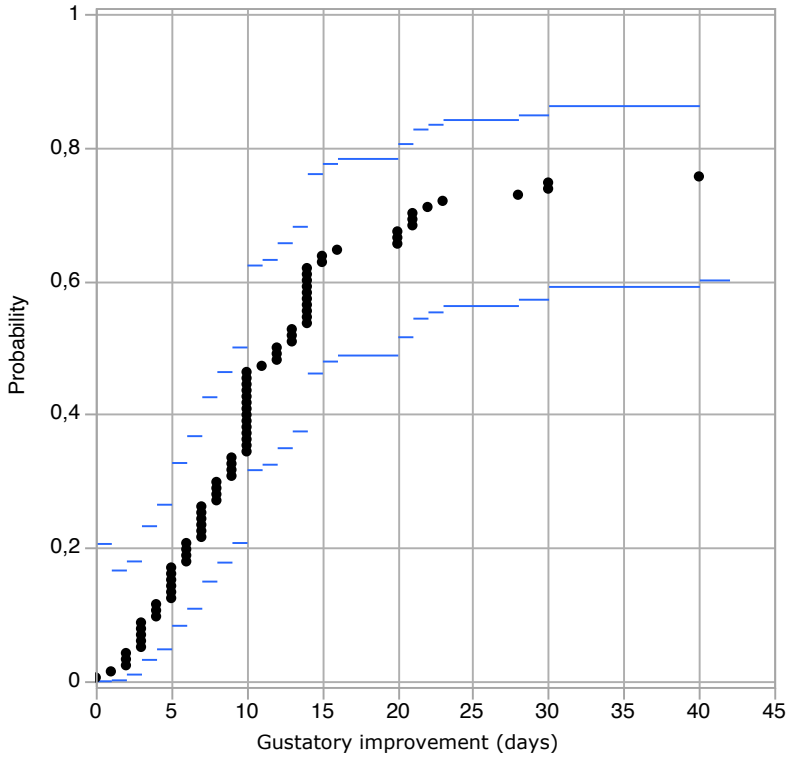
- Subjektivt lugtetab (tidligt):
  - 64% med lugtetab (yngre, mildt forløb, n=202) (Spinato, 2020)
  - 65% med lugtetab (n=6.452) (Menni, 2020)

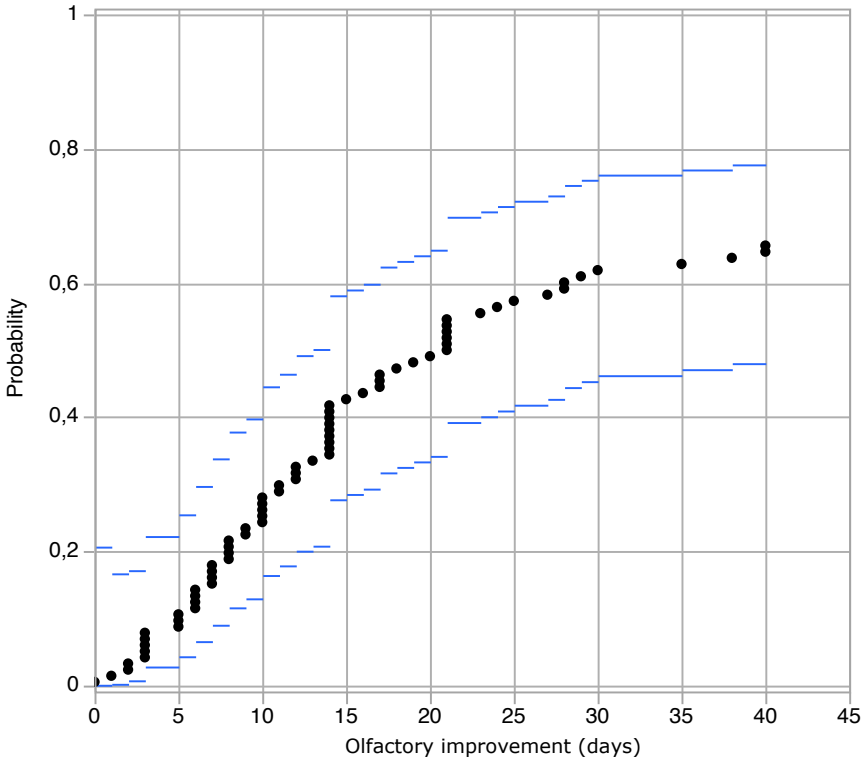
- Testverificeret lugtetab (tidligt):
  - Både lugte- og smagstab (Haldrup, 2020)
  - 98% med lugtetab (indlagte med COVID-19, n=60) (Moein, 2020)

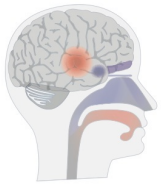


Lugte- og smagstab

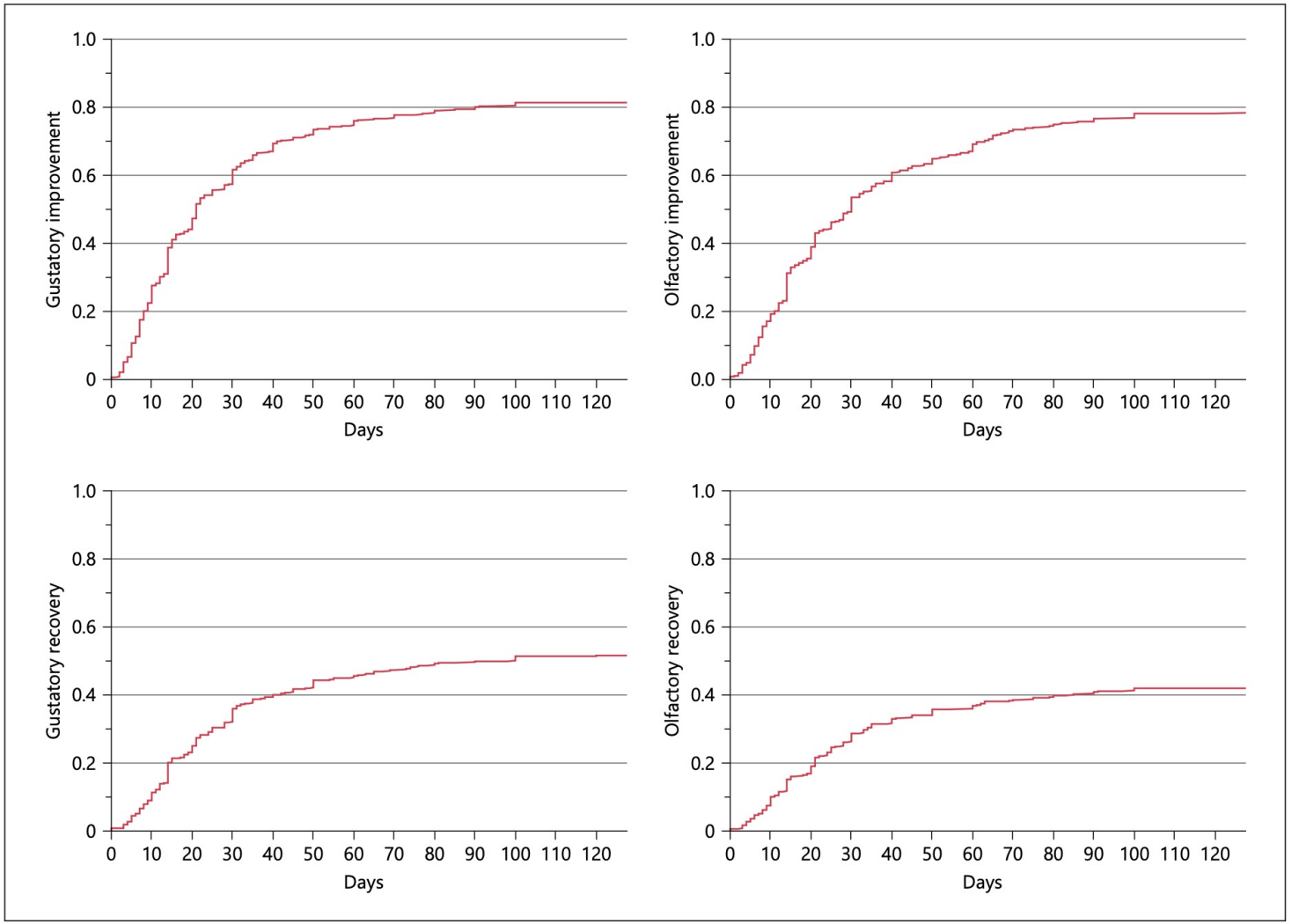
Varighed af COVID-19-sansetab



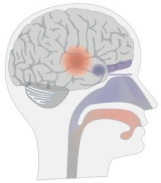




Varighed af COVID-19-sansetab



Schwab et al., ORL, 2021



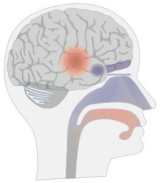
Hyppighed (præ-COVID-19)

Lugteforstyrrelser

- Subjektivt:
  - 4,5% (stigende med alder) (Lee, 2013)
  - 10,6% indenfor de sidste 12 måneder (Bhatt, 2015)
  - 23% har oplevet lugtetab i voksenlivet (Rawal, 2016)

- Testet:
  - 4,7% Anosmi og 15% hyposmi (Landis, 2004)
  - 3,6% Anosmi og 21,6% hyposmi (Vennemann, 2008)

- Nogle sygdomme giver øget forekomst (fx diabetes, nyresygdom)



Lugtetab

Årsager

Sino-nasal påvirkning
- Rhino-sinoitis (Akut/kronisk, med/uden polypper)
- Allergisk rhinitis
- Øvrig slimhindehævelse/påvirkning (fx graviditet)
- Nedsat passage (fx næsefraktur)

Postinfektiøst
- Øvre eller nedre luftveje
  - Direkte nerveskade (apoptose)
  - Fortsat hævelse/irritation

Posttraumatisk
- Nedsat passage
- Overrivning af filae olfactoriae
- Skade på cortex
- Blodansamling ved bulbus olfactorius

Central nervepåvirkning
- Apoplexi eller tumor (fx sulcus olfactorius, piriform cortex, temporallap, amygdala, limbisk system)
- Neurologisk sygdom (fx MS, ALS)
- Neurodegenerativ sygdom (fx PD, ALZ)

Iatrogent
- Lokal kirurgi (fx FESS, lokal analgesi (Moffats), hjernekirurgi)
- Generel anæstesi

Kongenit
- Syndromer (fx Kallmann syndrom, Klinefelter syndrom, CHARGE syndrom)
- Mange øvrige årsager (fx CMV)

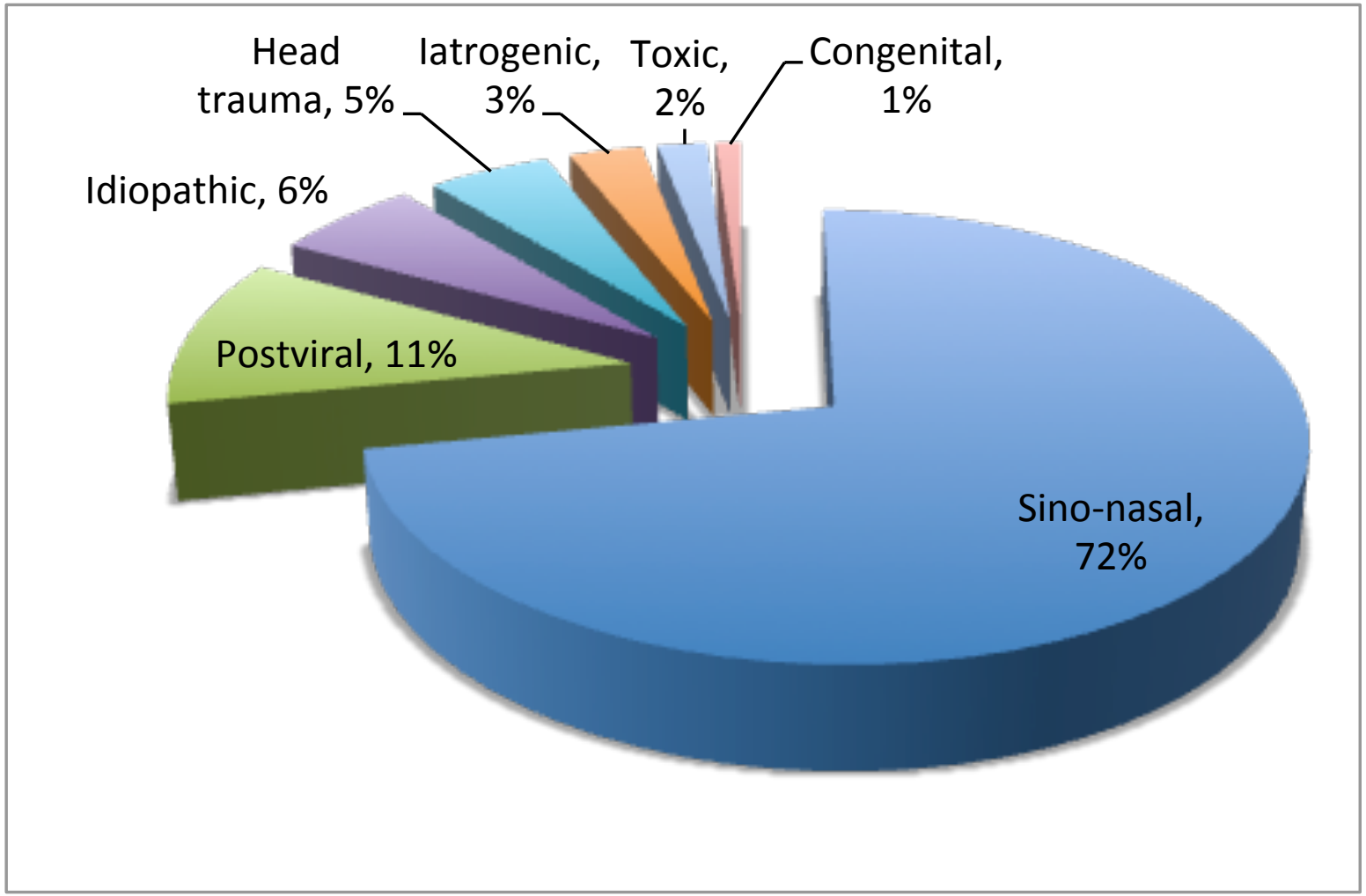
Bivirkninger og nerveskader
- Stråleterapi
- Kemoterapi
- Medicin (Fx antibiotika, antihypertensiv)
- Mad eller miljøtoksiner
- Rygning

Aldersrelateret

Psykologisk / psykiatrisk

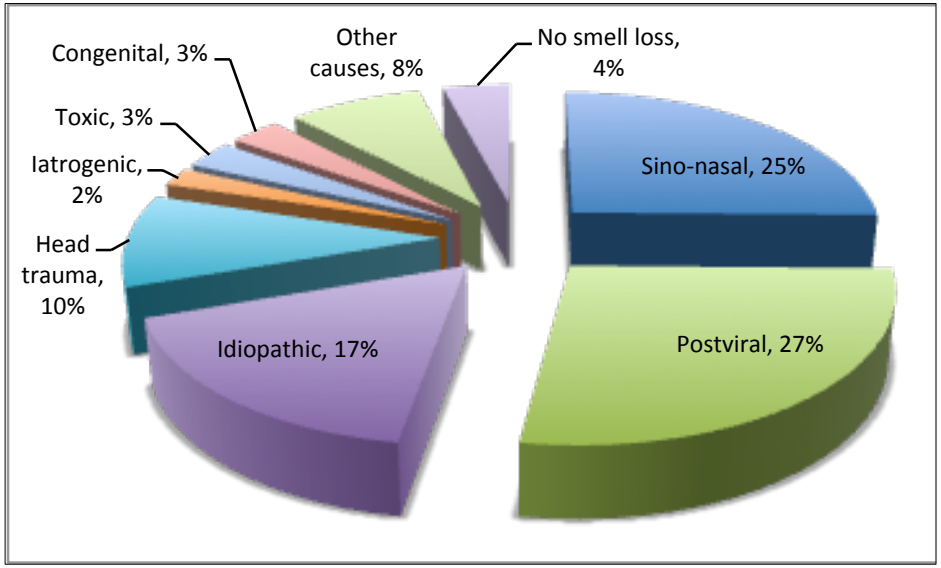
Idiopatisk

Årsager (primærsektor)

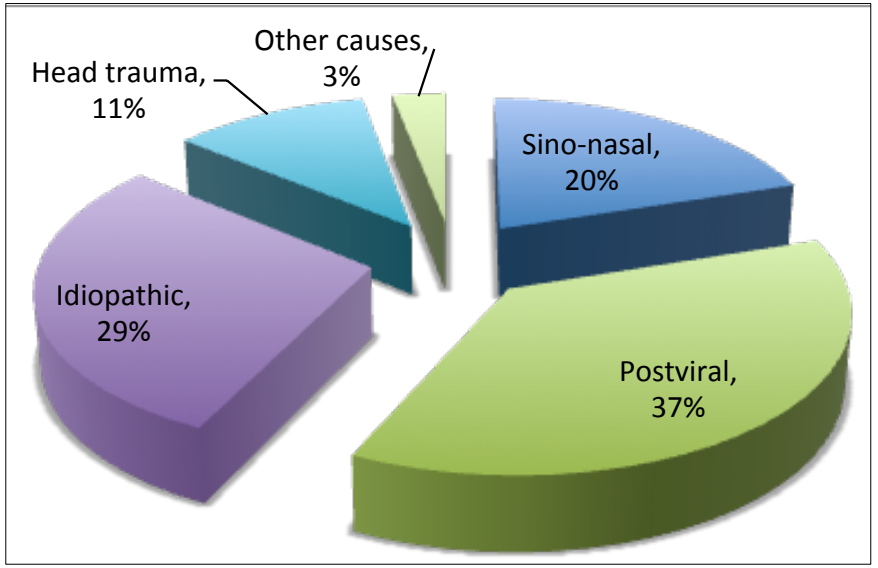


Damm et al, HNO, 2004 (Tyskland, Hospitaler og privat praksis)

Årsager (Flavour Klinikker)

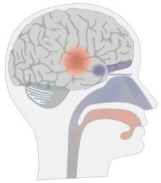


Danmark (Holstebro)



Tyskland (Køln)

Fjaeldstad et al., 2020.



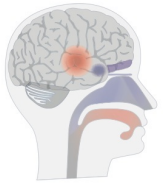
Postinfektiøst lugtetab

Tidligere

- Blandede virale infektioner
- Isoleret lugtetab
- Midaldrende patienter (gns. 62 år)

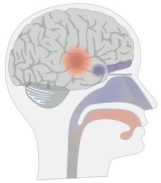
2020-21

- SARS-CoV2 dominerer
- Lugte- **og smagstab**
- Yngre patienter (gns. 40 år)



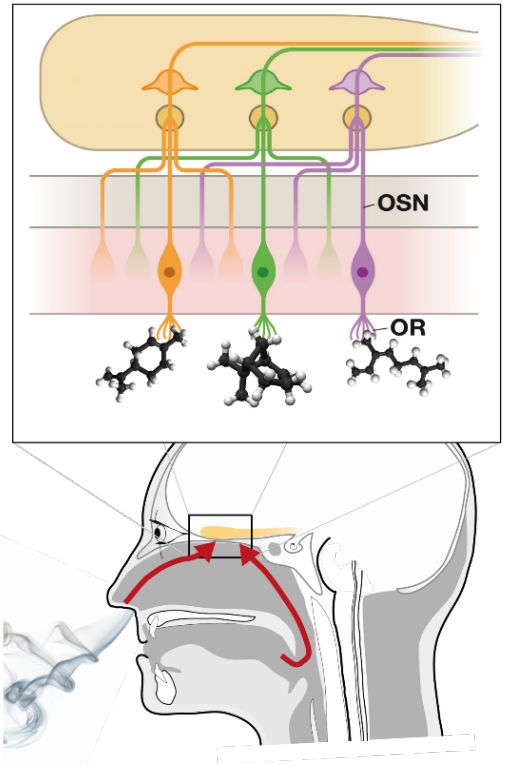
Ikke blot en reduktion af sansning

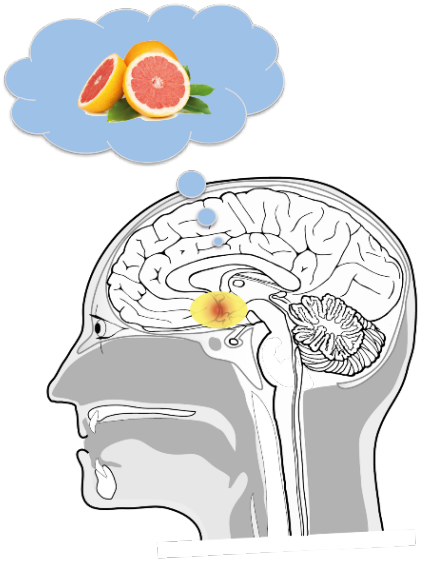
- Introduktion til termer
- Hvorfor er især lugtesansen ramt?
- Et multisensorisk problem
- Hvilke sanser er påvirkede?
- Mad og kostændringer ved COVID-19 sansetab



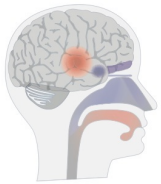
Overblik

Stimuli → Sansning → Perception

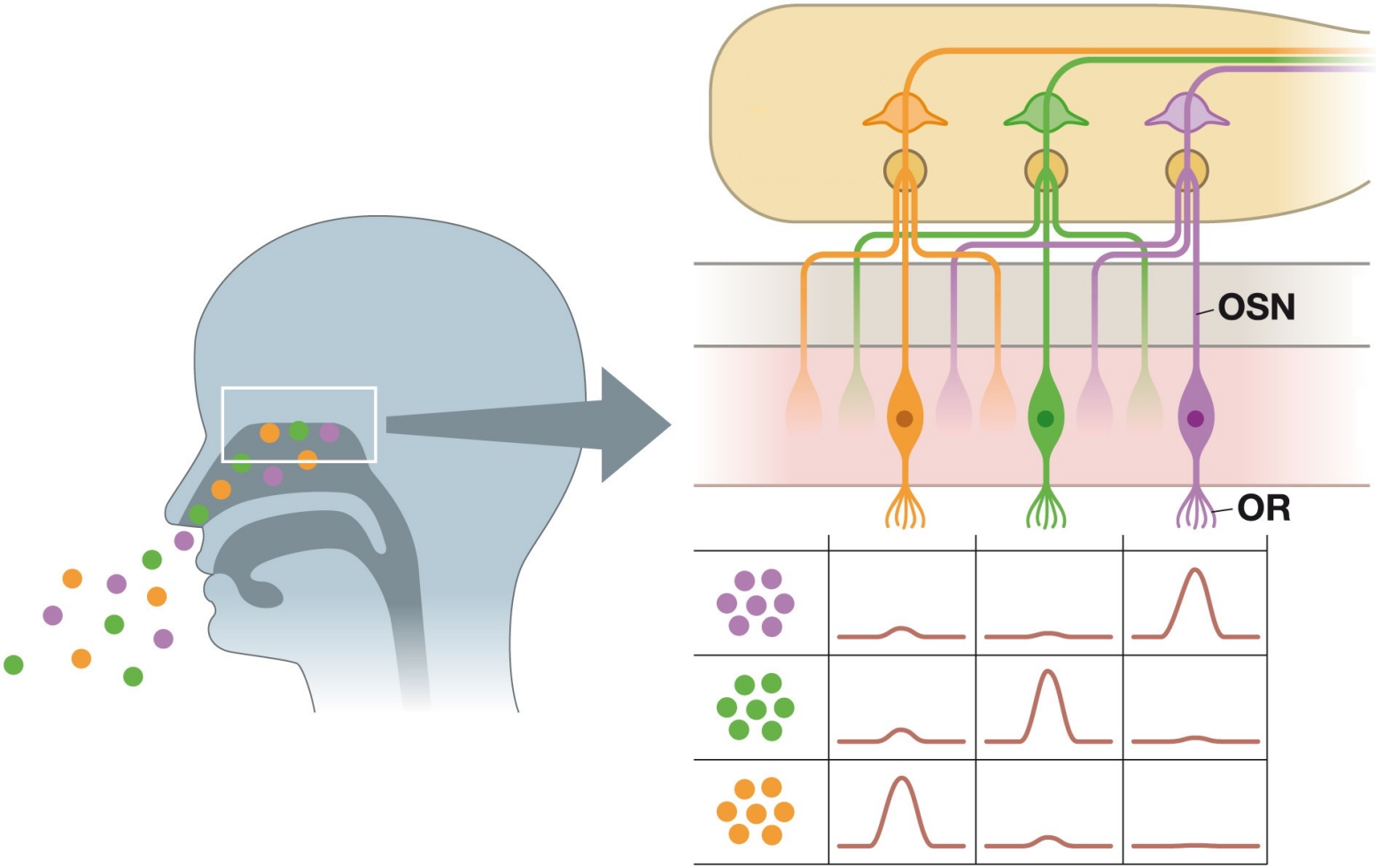




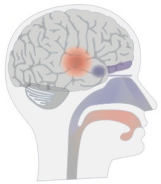
Fjaeldstad et al, Chem Percept, 2017



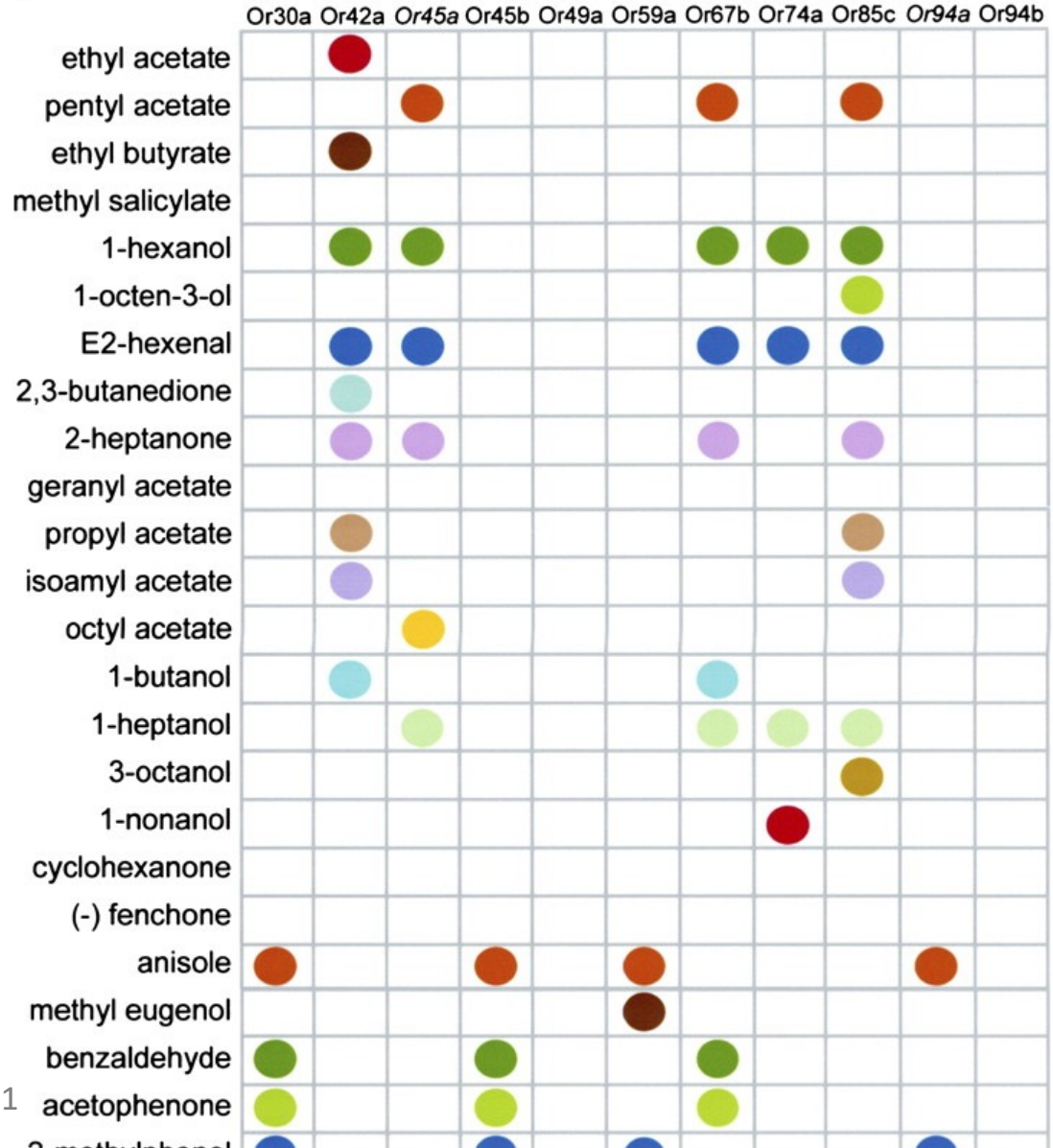
Aktivering af receptorer

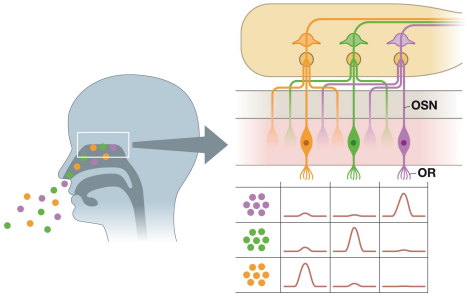


Fjaeldstad et al., 2014.



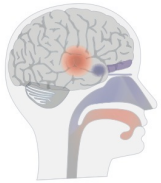
Olfaktoriske receptorer





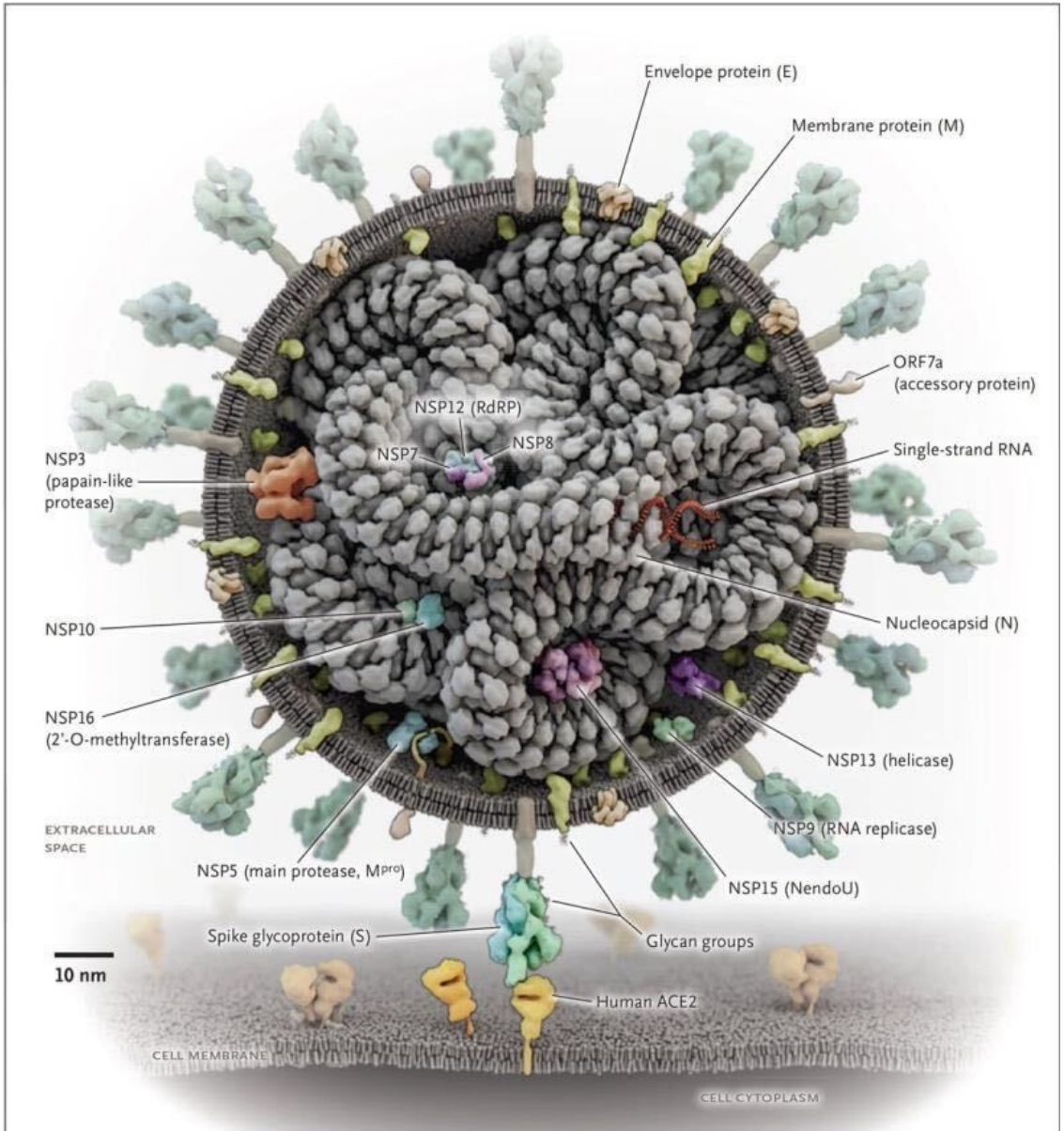
Carey. 2011

AARHUS UNIVERSITY

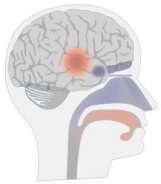


Lugtetab

COVID-19



Parks, NEJM, 2020



Lugtetab

COVID-19

nature medicine

BRIEF COMMUNICATION

https://doi.org/10.1038/s41591-020-0868-6

Check for updates

SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes

Waradon Sungnak[1]✉, Ni Huang[1], Christophe Bécavin[2], Marijn Berg[3,4], Rachel Queen[5], Monika Litvinukova[1,6], Carlos Talavera-López[1], Henrike Maatz[6], Daniel Reichart[7], Fotios Sampaziotis[8,9,10], Kaylee B. Worlock[11], Masahiro Yoshida[11], Josephine L. Barnes[11] and HCA Lung Biological Network*✉

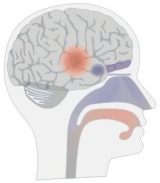
We investigated SARS-CoV-2 potential tropism by surveying expression of viral entry-associated genes in single-cell RNA-sequencing data from multiple tissues from healthy human donors. We co-detected these transcripts in specific respiratory, corneal and intestinal epithelial cells, potentially explaining the high efficiency of SARS-CoV-2 transmission. These genes are co-expressed in nasal epithelial cells with genes involved in innate immunity, highlighting the cells' potential role in initial viral infection, spread and clearance. The study offers a useful resource for further lines of inquiry with valuable clinical samples from COVID-19 patients and we provide our data in a comprehensive, open and user-friendly fashion at www.covid19cellatlas.org.

The coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. Detection of the virus was first reported in Wuhan[2], China and has since spread worldwide, emerging as a global pandemic[3].

associated with SARS-CoV-2 pathogenesis at cellular resolution, using single-cell RNA sequencing (scRNA-seq) datasets from healthy donors generated by the Human Cell Atlas consortium and other resources to inform and prioritize the use of precious, limited clinical material that is becoming available from COVID-19 patients.

We investigated gene expression of *ACE2* in multiple scRNA-seq datasets from different tissues, including those of the respiratory tree, cornea, retina, esophagus, ileum, colon, heart, skeletal muscle, spleen, liver, placenta/decidua, kidney, testis, pancreas, prostate gland, brain, skin and fetal tissues. We note that studies may lack specific cell types due to their sparsity, the challenges associated with isolation or analysis methodology. Moreover, expression may be under-detected due to technical dropout effects. Thus, while positive (presence) results are highly reliable, absence should be interpreted with care.

ACE2 expression was generally low in all analyzed datasets. Consistently with independent studies[10,11], *ACE2* was expressed in



Lugtetab

COVID-19

nature medicine

BRIEF COMMUNICATION

https://doi.org/10.1038/s41591-020-0916-2

Check for updates

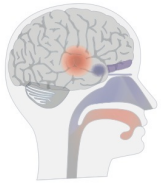
Real-time tracking of self-reported symptoms to predict potential COVID-19

Cristina Menni[1,7]✉, Ana M. Valdes[1,2,7], Maxim B. Freidin[1], Carole H. Sudre[3], Long H. Nguyen[4], David A. Drew[4], Sajaysurya Ganesh[5], Thomas Varsavsky[3], M. Jorge Cardoso[3], Julia S. El-Sayed Moustafa[1], Alessia Visconti[1], Pirro Hysi[1], Ruth C. E. Bowyer[1], Massimo Mangino[1,6], Mario Falchi[1], Jonathan Wolf[5], Sebastien Ourselin[3], Andrew T. Chan[4], Claire J. Steves[1,8] and Tim D. Spector[1,8]✉

A total of 2,618,862 participants reported their potential symptoms of COVID-19 on a smartphone-based app. Among the 18,401 who had undergone a SARS-CoV-2 test, the proportion of participants who reported loss of smell and taste was higher in those with a positive test result (4,668 of 7,178 individuals; 65.03%) than in those with a negative test result (2,436 of 11,223 participants; 21.71%) (odds ratio = 6.74; 95% confidence interval = 6.31–7.21). A model combining symptoms to predict probable infection was applied to the data from all app users who reported symptoms (805,753) and predicted that 140,312 (17.42%) participants are likely to have COVID-19.

COVID-19 is an acute respiratory illness caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Since its outbreak in China in December 2019, als and tracks in real time how the disease progresses by recording self-reported health information on a daily basis, including symptoms, hospitalization, reverse-transcription PCR (RT-PCR) test outcomes, demographic information and pre-existing medical conditions.

Between 24 March and 21 April 2020, 2,450,569 UK and 168,293 US individuals reported symptoms through the smartphone app. Of the 2,450,569 participants in the United Kingdom, 789,083 (32.2%) indicated having one or more potential symptoms of COVID-19 (Table 1). In total, 15,638 UK and 2,763 US app users reported having had an RT-PCR SARS-CoV-2 test, and having received the outcome of the test. In the UK cohort, 6,452 participants reported a positive test and 9,186 participants had a negative test. In the cohort from the United Kingdom, of the 6,452 participants who tested



Lugtetab

COVID-19

Table 1 | Characteristics of the study population

	Tested for SARS-CoV-2				Not tested for SARS-CoV-2	
	United Kingdom		United States		United Kingdom	United States
	Tested positive	Tested negative	Tested positive	Tested negative		
Number	6,452	9,186	726	2,037	2,434,931	165,530
Female (%)	71.88	76.40	78.10	82.28	64.24	68.67
Age (years)	41.25 (12.18)	41.87 (12.14)	44.65 (14.31)	47.25 (13.80)	43.38 (14.69)	53.00 (16.68)
BMI ($kg\,m^{-2}$)	27.34 (6.06)	27.04 (5.91)	28.04 (6.91)	27.71 (636)	26.39 (5.44)	27.08 (5.87)
Answered questions on symptoms (*n*)	6,452	9,186	726	2,037	773,539	32,214
Loss of smell and taste (%)	64.76	22.68	67.49	17.33	9.50	12.10
Fatigue (%)	29.80	15.56	23.42	21.50	8.71	8.17
Shortness of breath (%)	15.27	9.37	13.50	12.03	4.52	3.65
Fever (%)	34.34	23.93	27.74	26.25	9.31	4.78
Persistent cough (%)	56.73	45.56	44.77	41.24	30.17	22.25
Diarrhea (%)	25.95	19.24	32.92	29.06	19.33	23.26
Delirium (%)	17.87	13.25	23.55	23.47	15.26	16.25
Skipped meals (%)	42.03	24.93	47.25	36.08	19.12	21.42
Abdominal pain (%)	21.31	18.24	20.94	21.06	3.70	15.94
Chest pain (%)	42.73	39.17	38.57	41.92	18.65	24.74
Hoarse voice (%)	31.70	25.85	26.86	25.72	7.86	13.79

The results are presented as percentage values for dichotomous traits and as means and standard deviation (in parentheses) for continuous traits (age and BMI).

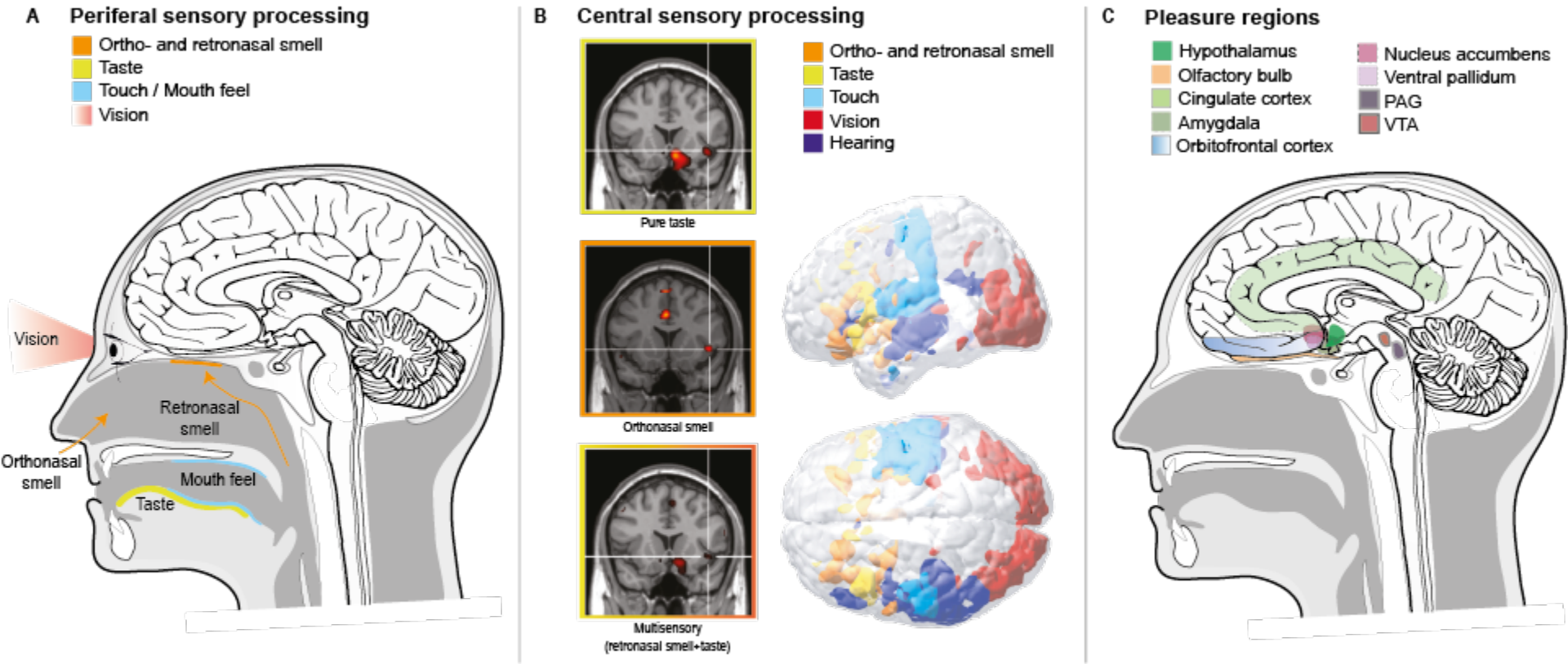
Menni, Nature Med., 2020

midt Central Denmark Region

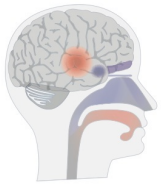
AARHUS UNIVERSITY

Sensoriske senfølger ved COVID-19

Et multisensorisk problem

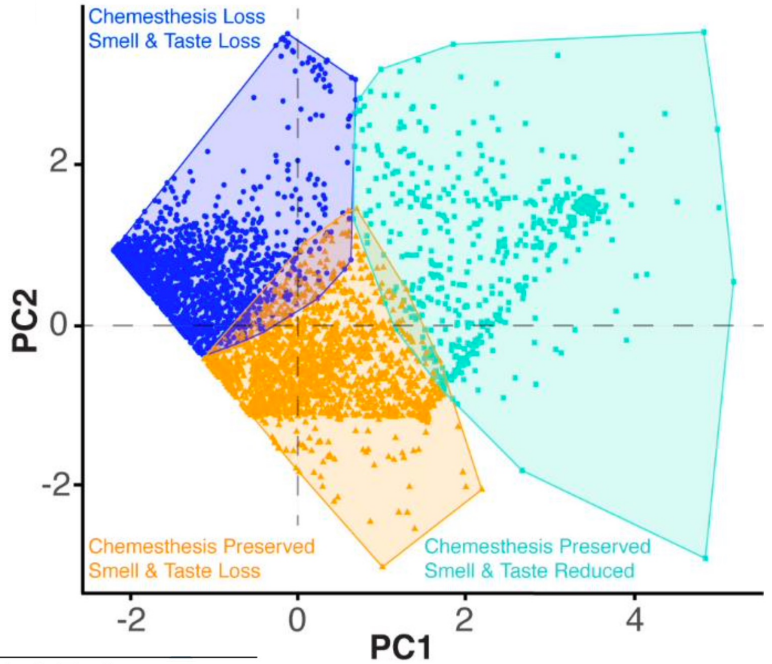


Fjaeldstad et al., Multisensory Flavour Perception, 2016



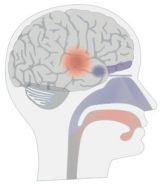
Et multisensorisk problem

- Lugtesansen
- Smagssansen
- Trigeminal sansning



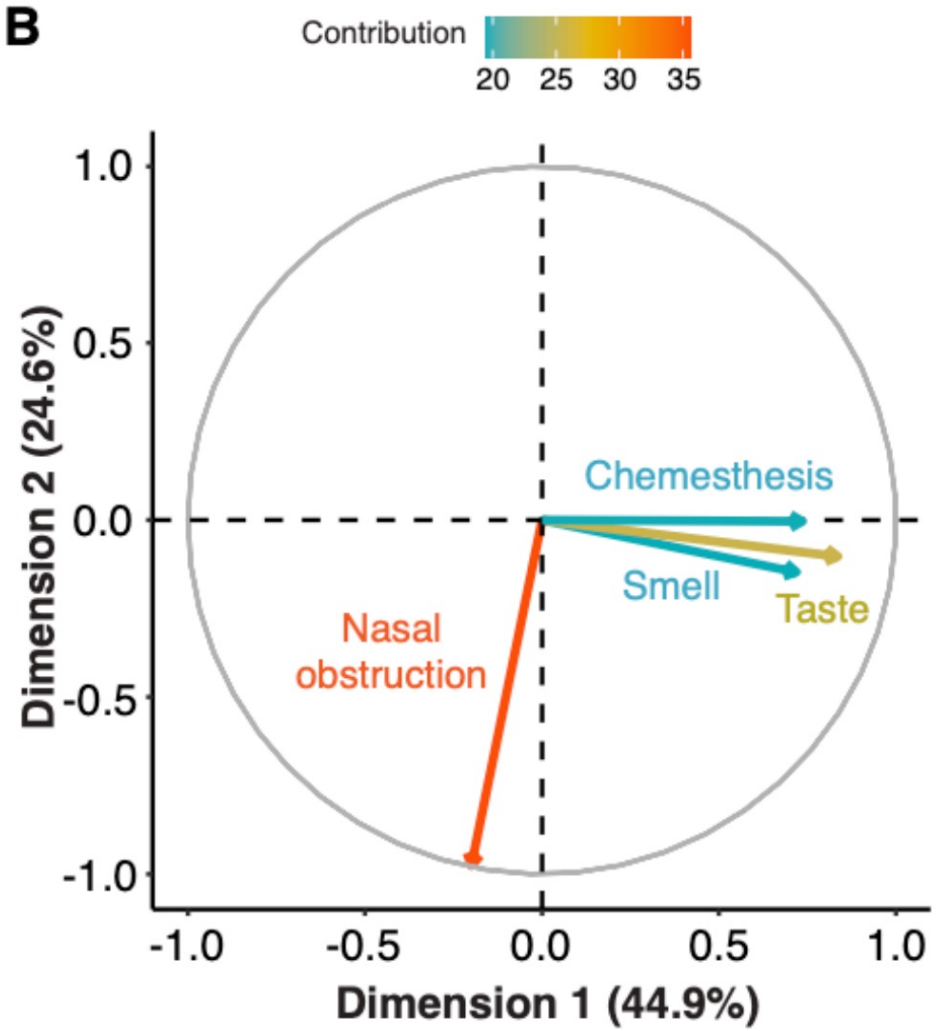
	Clinical Assessment				Lab Test			
	Before COVID-19		During COVID-19		Before COVID-19		During COVID-19	
Variable	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Smell	90.18	14.92	11.49	24.24	90.96	15.71	9.46	22.33
Taste	91.33	13.25	23.34	29.36	92.00	14.34	21.23	28.71
Chemesthesis	84.96	18.74	47.48	32.17	83.72	22.1	46.68	32.2
Nasal Obstruction	9.83	18.41	31.67	32.11	9.35	17.89	32.67	31.62

Parma et al., Chem Sens, 2020

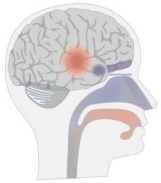


Lugtetab

COVID-19

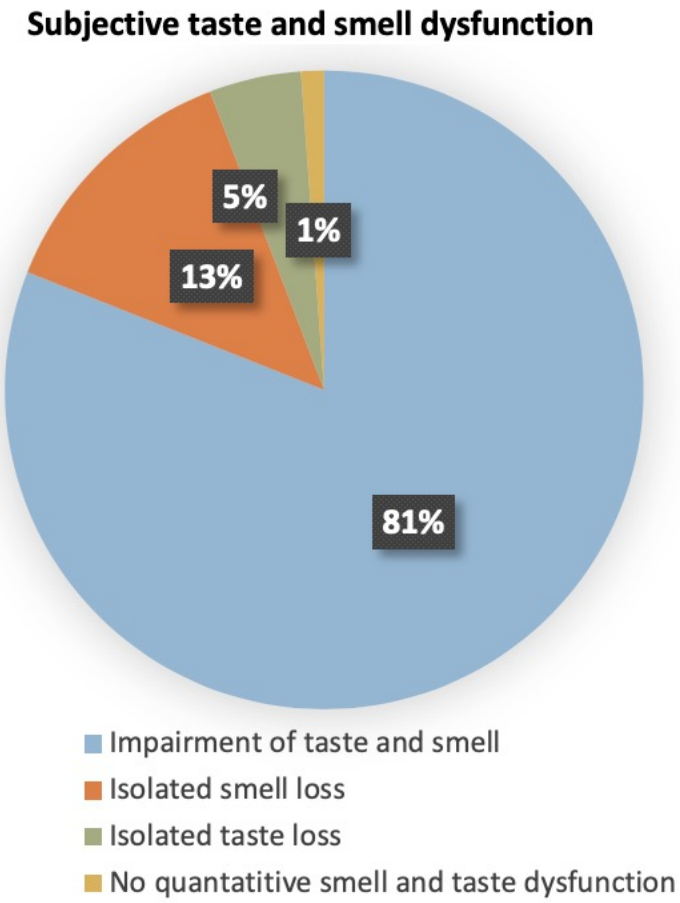


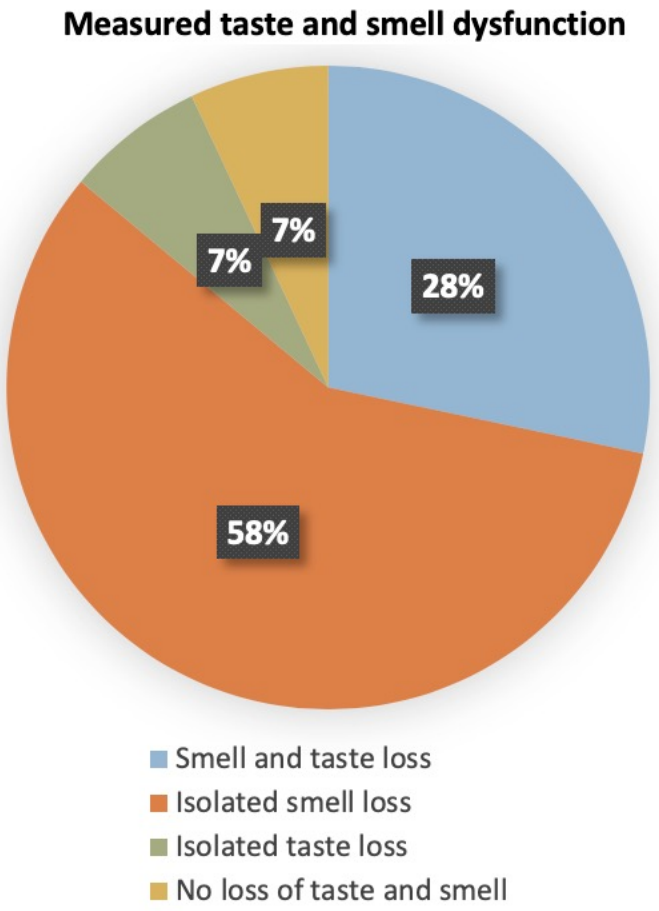
Parma. 2020



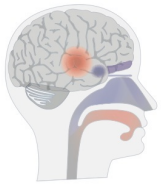
Lugte- og smagstab

Hvorfor testning?





Nørgaard et Fjaeldstad, ORL, 2021

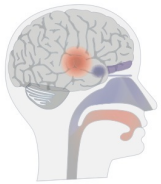


Lugte- og smagstab

Simpel testning

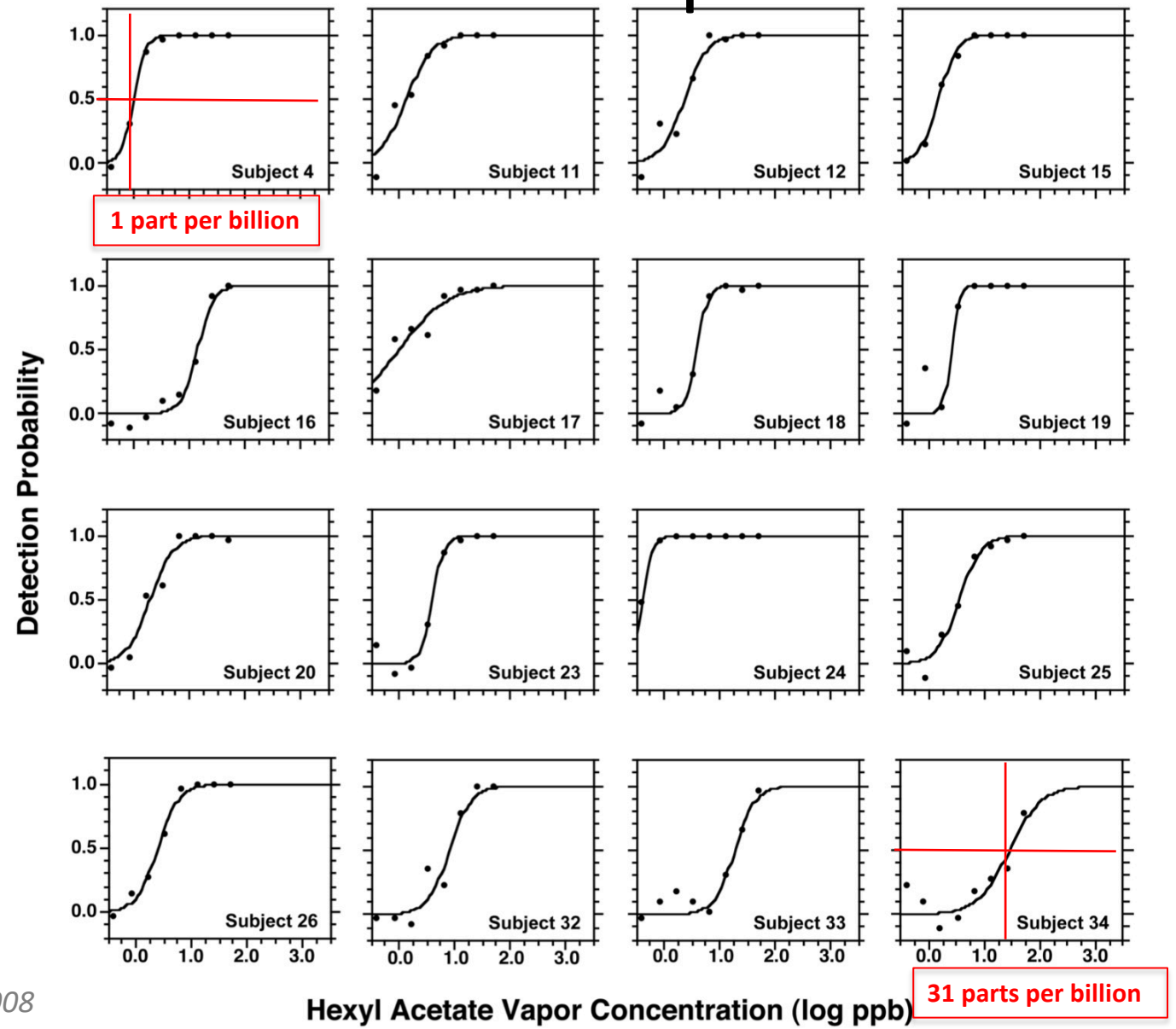
midt
Central Denmark Region

AARHUS UNIVERSITY

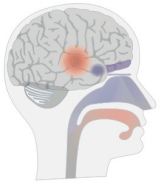


Lugte- og smagstab

Intet er helt simpelt



Cometto-Muniz. 2008



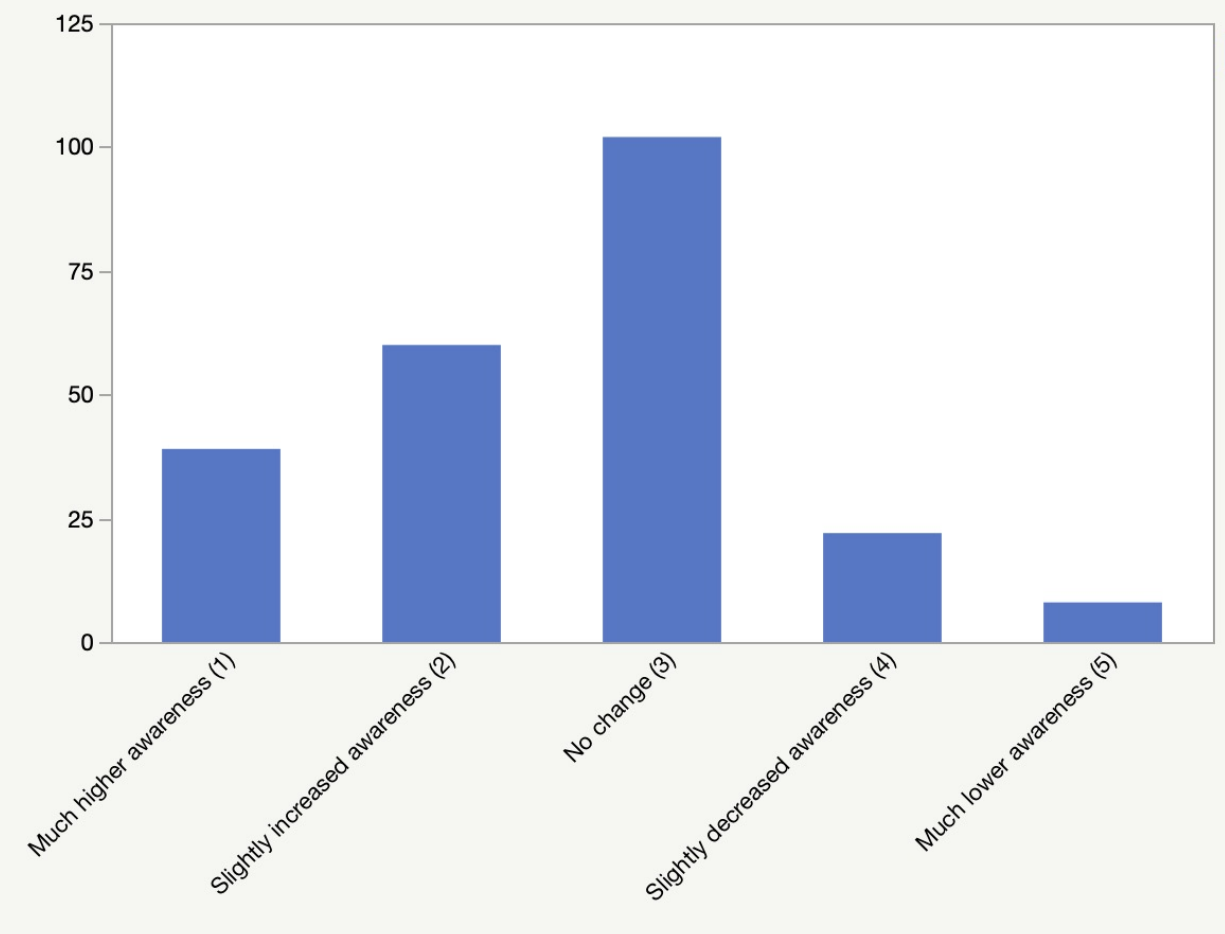
Trigeminale effekter

- Tab af trigeminal sensitivitet reducerer olfaktorisk funktion [1]
- Trigeminal aktivering er øget på slimhindeniveau hos patienter med erhvervet anosmi – dog er de centrale signaler svagere [2]

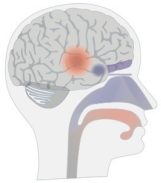
CO^2

1. Husner, 2006; 2. Frasnelli, 2007.

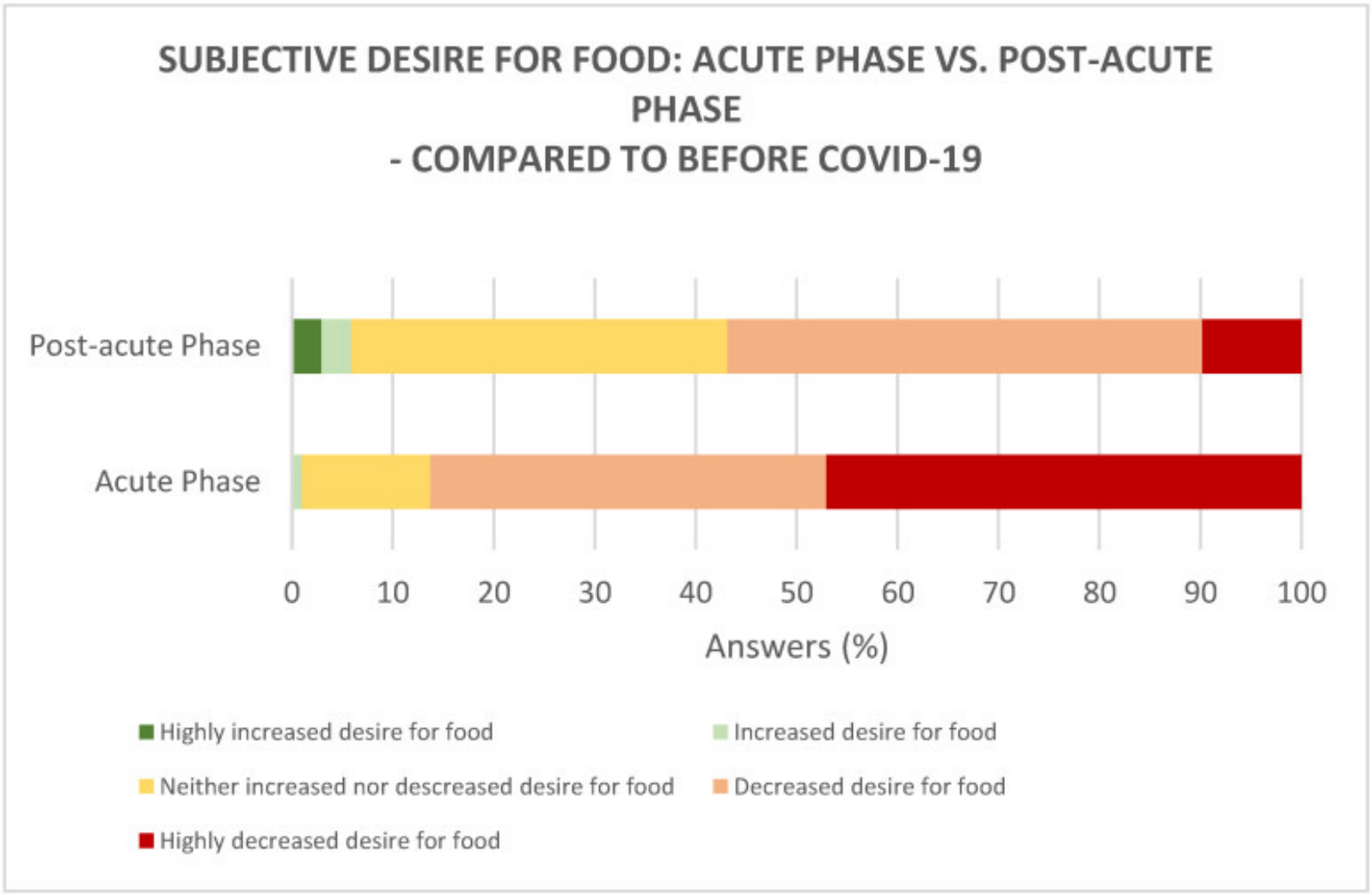
Trigeminale senfølger ved COVID-19



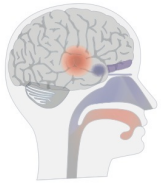
Fjaeldstad et al., (unpublished data), n=263



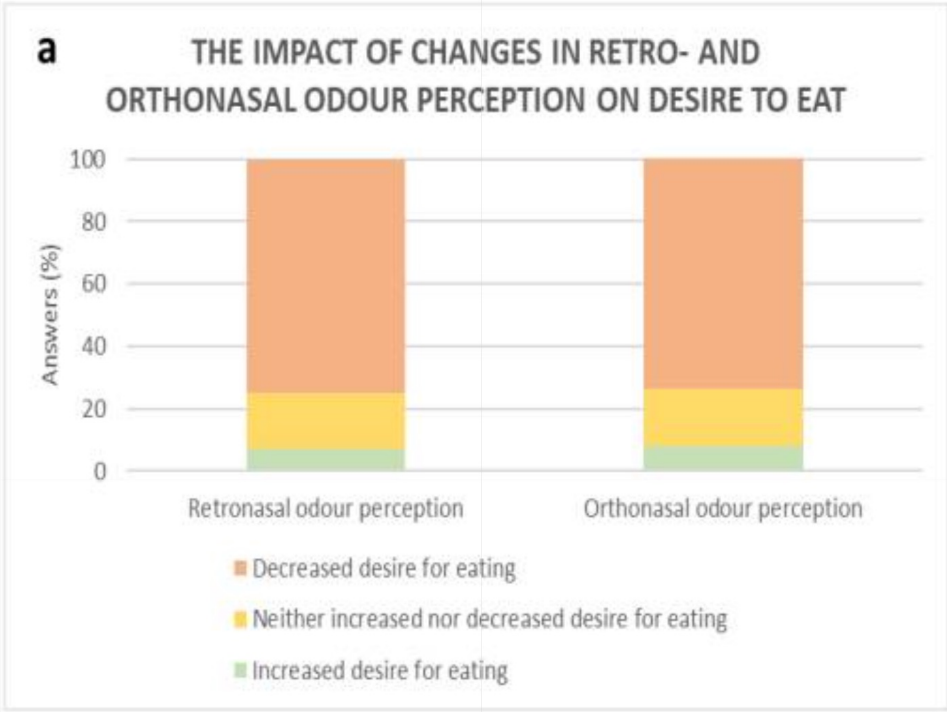
Mad og kostændringer

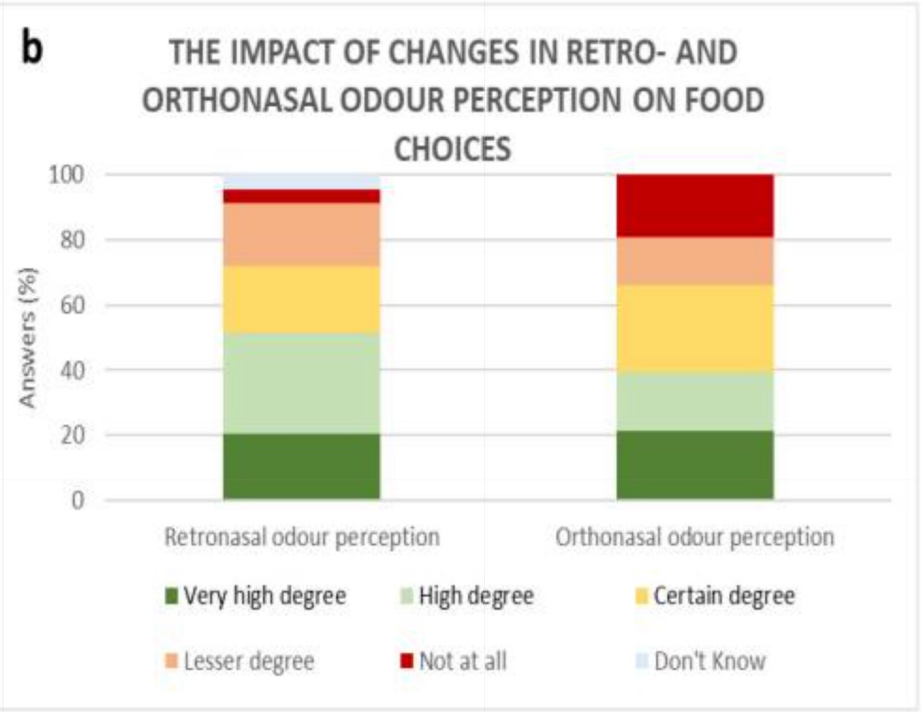


Chaaban et al., Foods, 2021

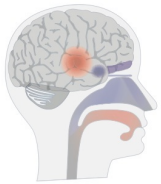


Mad og kostændringer



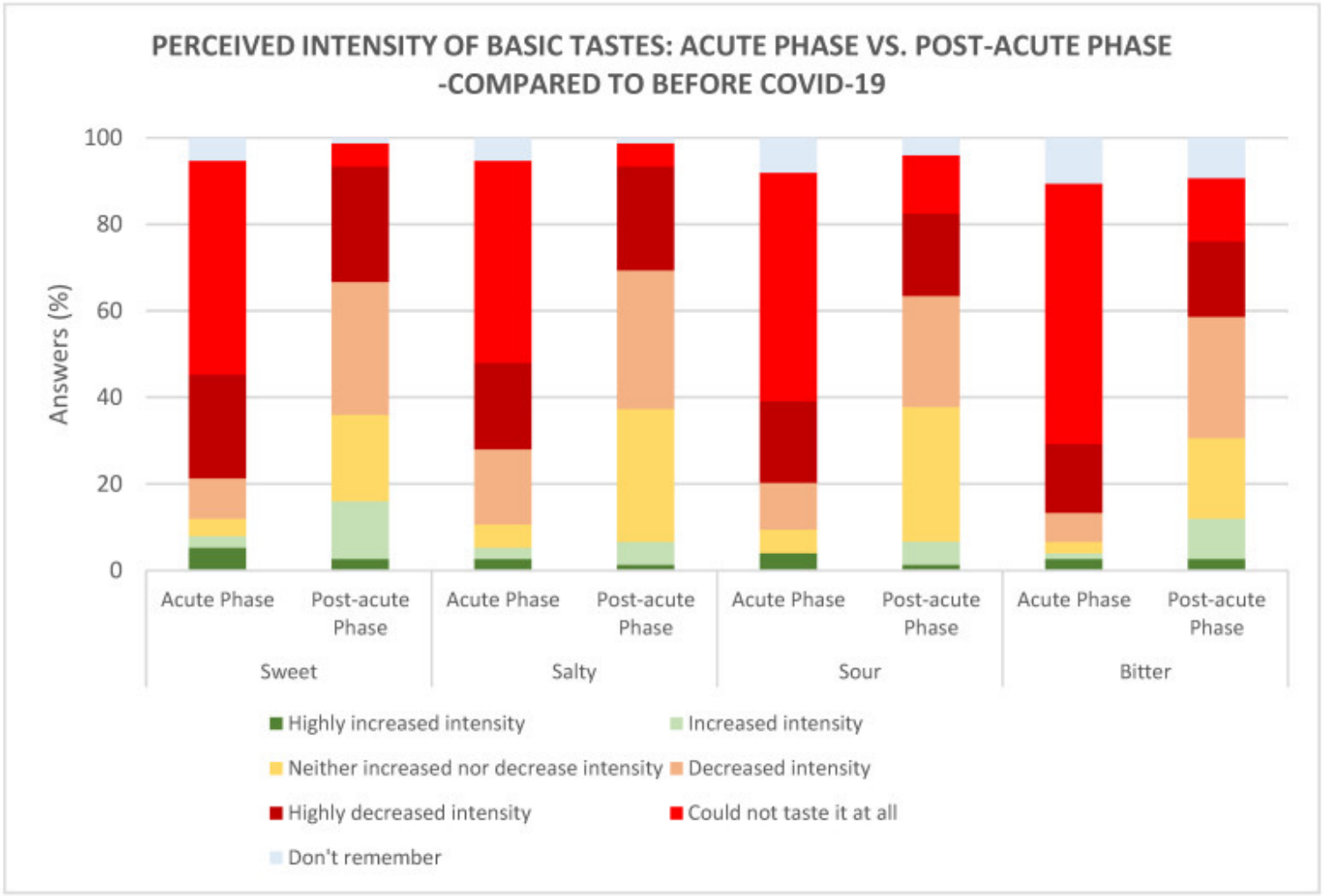


Chaaban et al., Foods, 2021



Smagstab

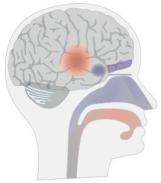
Mad og kostændringer



Chaaban et al., Foods, 2021

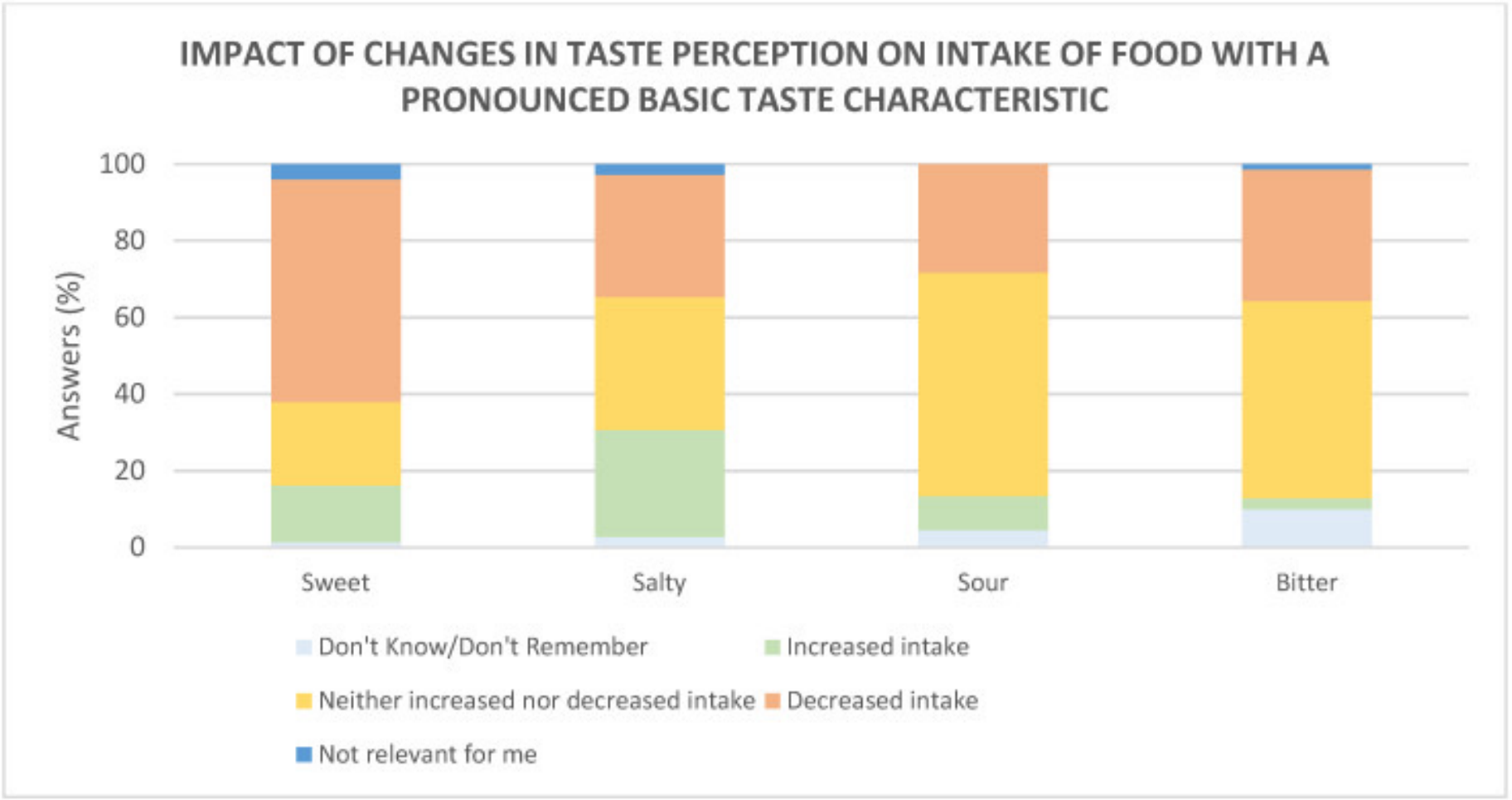
midt Central Denmark Region

AARHUS UNIVERSITY

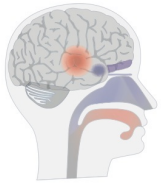


Smagstab

Mad og kostændringer

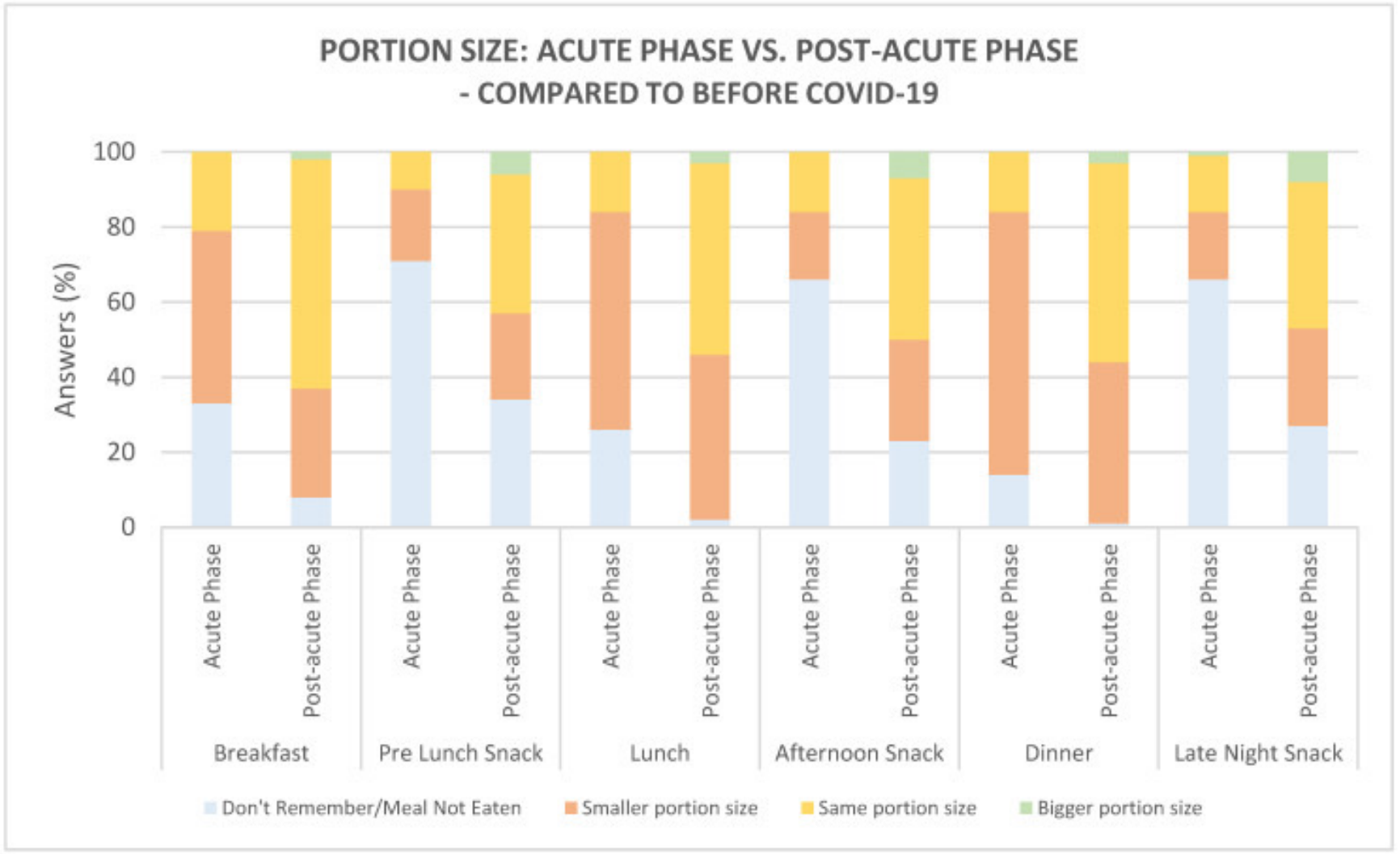


Chaaban et al., Foods, 2021



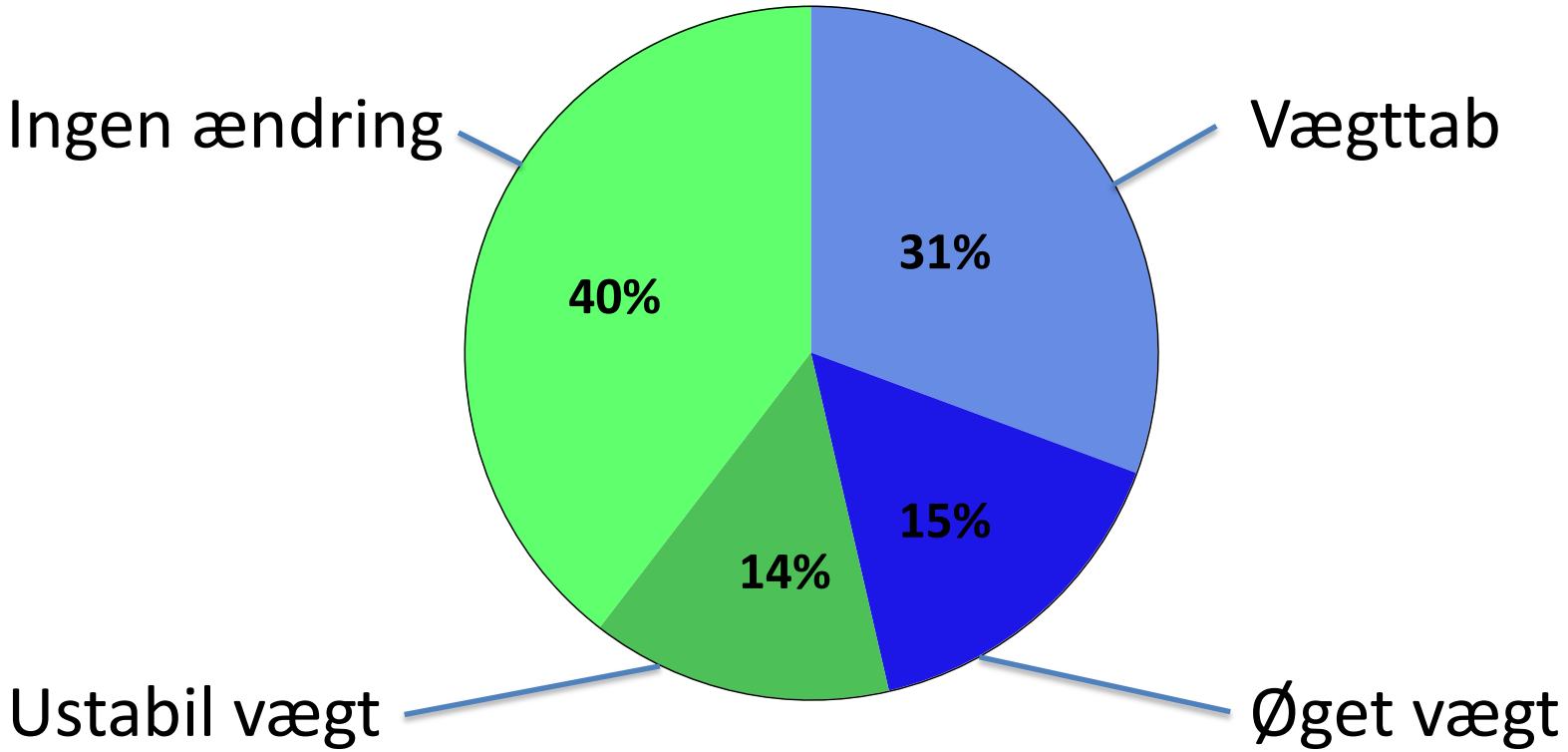
Lugte- og smagstab

Mad og kostændringer

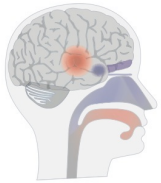


Chaaban et al., Foods, 2021

Ændringer i vægt efter COVID-19



Fjaeldstad et al., (unpublished data), n=263



Vejledning til patienters madlavning

Hyposmi/anosmi

- Krydret mad (karry, barbecue, krydderurter)
- Stimuler de øvrige sanser
  - Temperatur forskelle
  - Tekstur forskelle
  - Taktilitet
  - Trigeminale stimuli

Parosmi

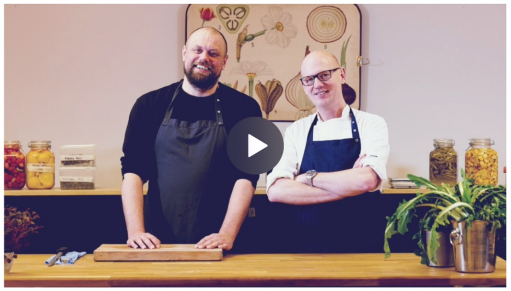
- Kolde/kølige madvarer
- Spis 'Ikke-aromatisk' mad: ris, nudler, youghurt natural, uristet brød, dampede grøntsager
- Undgå: stegt kød og anden mad med stegeskorpe, løg, hvidløg, kaffe, æg, chokolade

Flavour Klinikken

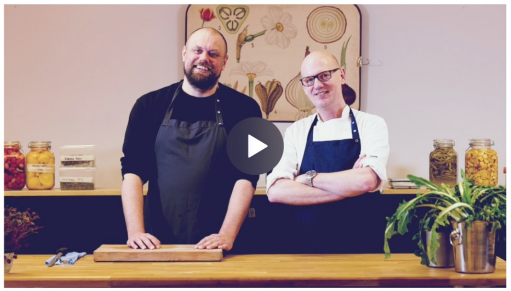
Vejledning til patienters madlavning

Mad med lugtetab – Introduktion

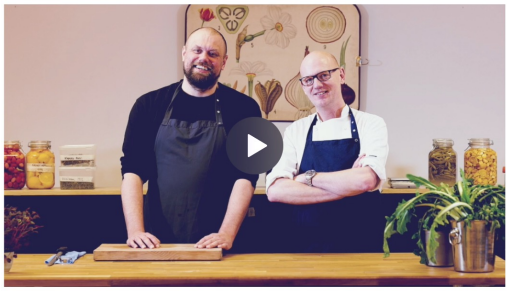
Mad med lugtetab – Smagekit



Mad med lugtetab – Tekstur



Mad med lugtetab – Taktilitet



Mad med lugtetab – Trigeminal Smerte

www.Flavourinstitute.dk

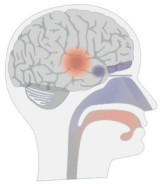
https://www.youtube.com/

VELUX FONDEN

midt Central Denmark Region

Flavour Institute & Flavour Klinikken; Christian Bøjlund og Rasmus Bredahl

AARHUS UNIVERSITY



Hovedbudskaber

- Lugtetab er det hyppigste symptom på COVID-19, hvor smagssansen oftest også er påvirket
- De sensorisk senfølger kan være permanenter, men ændres ofte kvantitativt og kvalitativt over uger til måneder
- Testning af sanserne er at foretrække - især subjektivt smagstab er usikkert
- Øvrige sanser kan også være påvirkede
- Sansetab har ofte stor indflydelse på mad og madvaner

Alexander Fjældstad
Flavour Klinikken, ØNH, HEV