

# COVID-19 and stress : consequences for the *PERI orbital area*

Patrizia A d'Alessio MD PhD

ARCADIA



\* *No conflict of interest*

# Mood reflection in the peri-orbital area

happy



angry



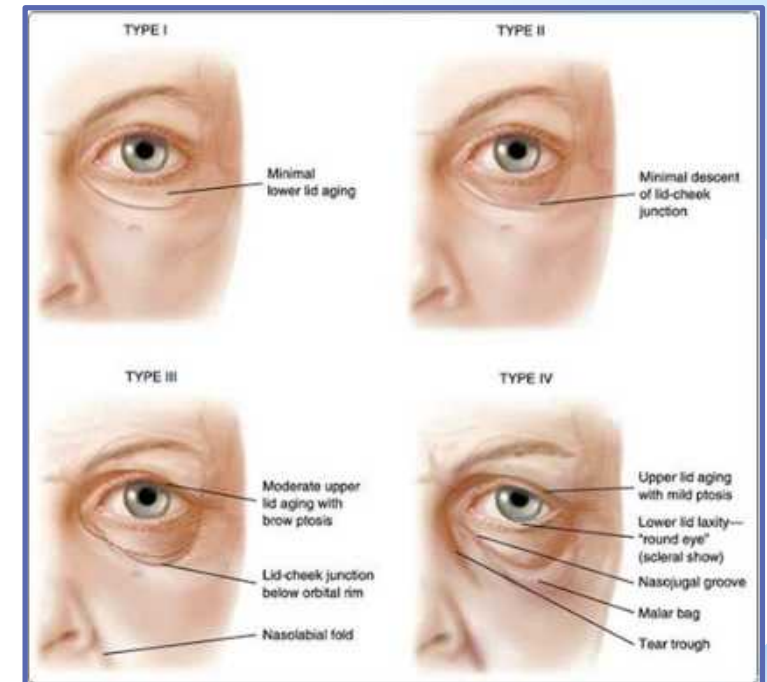
This is basically what we are left with...  
.. so frustrating!

# Peri orbital area is ONE of the first to show signs of aging & grief

due to volume depletion of the soft tissue and bone resorption,

as well as **stress** and issues of social inequality,

interventional but also **nonsurgical**, office-based procedures are important for overall peri orbital rejuvenation.



# Is Covid-19 more than a pandemic ?

« *Two categories of diseases are interacting within specific populations—*

- ◆ *infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and*
- ◆ *an array of non-communicable diseases (NCDs).*

*These conditions are clustering within social groups according to **patterns of inequality** deeply embedded in our societies. »*



The screenshot shows a Lancet article page. At the top, there is a blue banner with the text "Every region." and "THE LANCET Regional Health". Below this, the Lancet logo is visible. The article title is "Offline: COVID-19 is not a pandemic" by Richard Horton. The publication date is September 26, 2020. There is a "Check for updates" button.

« The economic crisis that is advancing towards us **will not be solved** by a drug or a vaccine. »

# Could COVID-19 be a syndemic?

The total number of people with **chronic diseases** is growing

« **Syndemics** are characterised by **biological and social interactions** ... that increase a person's susceptibility to harm or worsen their health outcomes. »

« The aggregation of these diseases on a background of social and economic disparity **exacerbates the adverse effects** of each separate disease. »



WHAT  
TO DO?

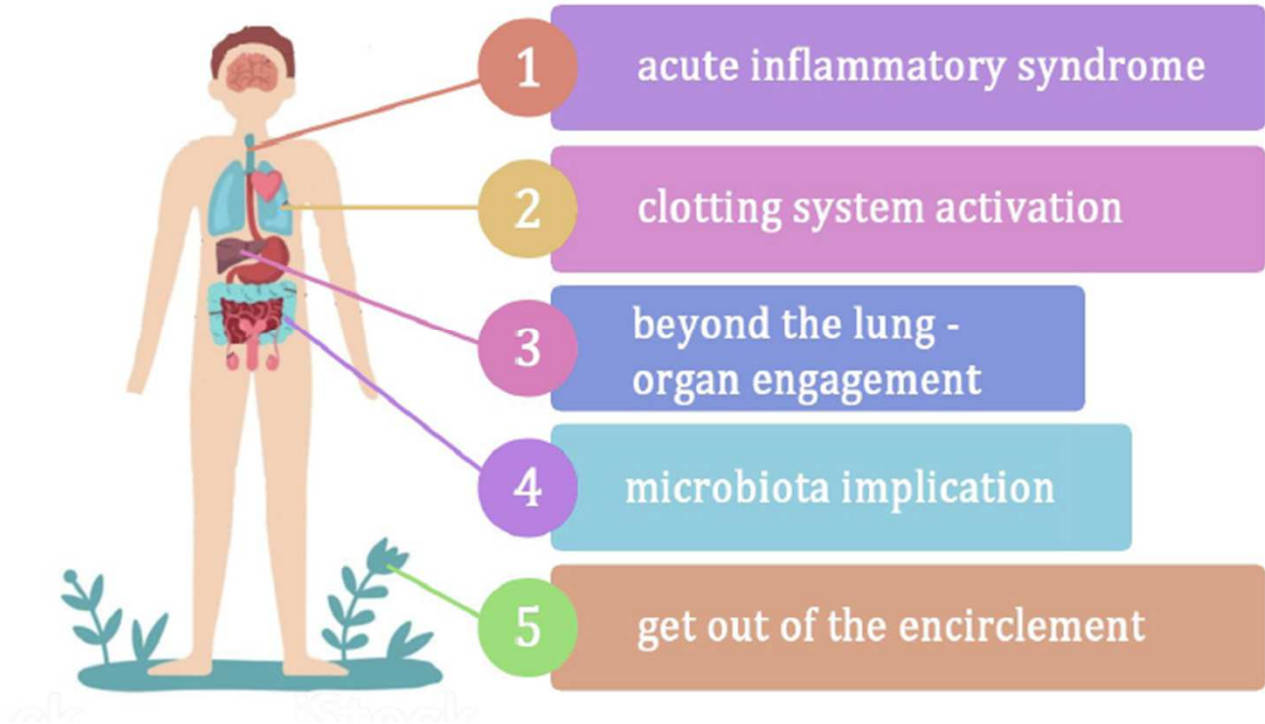
# Is there an UNDERLYING stress issue ?

- ◆ In SARS-CoV-2 infection the main cause of death,
- ◆ has been considered to be an **over reaction of the immune system** :

« **cytokine storm** »

associated to DIVC

(« disseminated intravascular coagulation »)



# « Cytokine storm »

**Acute inflammatory reaction involving HIGH LEVELS of IL-6, IL-1, TNF- $\alpha$  and interferons**

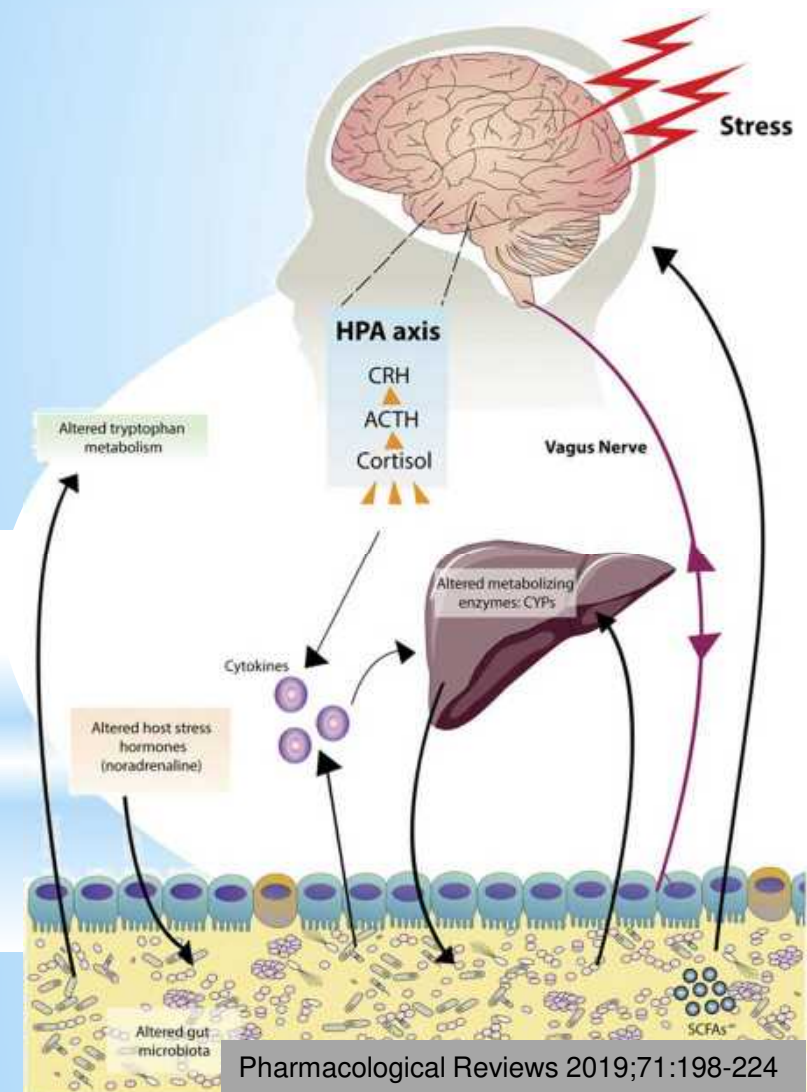
*“The fact that some studies have shown elevated levels of these inflammation-inducing cytokines in the blood of hospitalized COVID-19 patients, has drawn to the conclusion that the real morbidity and mortality of this disease is probably driven by **this out-of-proportion inflammatory response** to the virus...”*

(Jamie Garfield, Temple University Hospital)





# Stress coping mechanisms induce generalized inflammation



- ◆ Stress management is introducing a dangerous imbalance in the gut-brain connection,
- ◆ leading to dysbiosis, generalized inflammation with the appearance of the « sickness disease » syndrome, recognizable by :
- ◆ depression, lack of concentration, **loss of appetite for social interaction**, obsessional thoughts, chronic fatigue syndrome, anxiety, sleeplessness...

# When routes of stress CROSS those of the immune response

◆ Is SARS-CoV-2 infection taking advantage of our **stress** ?

◆ In case of chronic stress, when symptoms start to appear, we are **already** experiencing a « cytokine storm » close to chronic disease



# When does SOCIAL interaction enter the picture?

- ◆ This pandemic has also highlighted the importance of social interaction, crucial for maintaining good health.



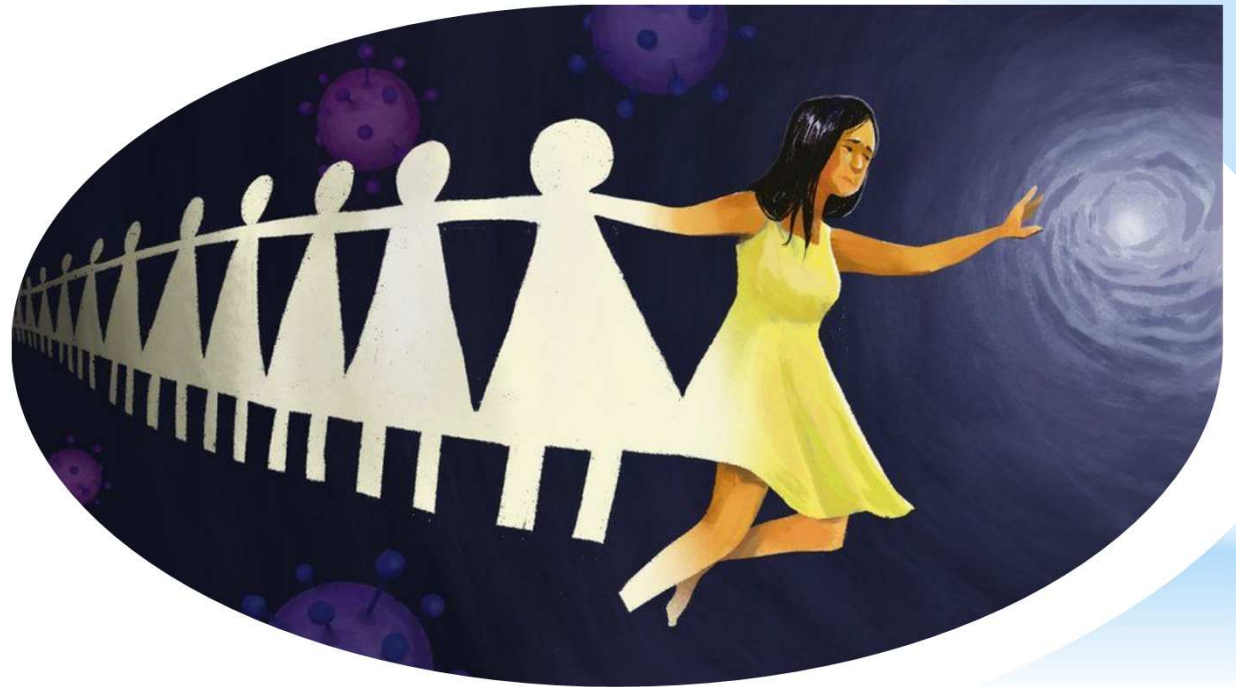
# \* In Japan a « Ministry of SOLITUDE »

In the country of longevity, of centenarians, blue zone and healthy rice and fish diet ...

In October 2020 ... after six months restrictions

\* **70% increase in female suicides compared to October 2019**

Do **social restriction policies** overimpose stress on an already stressed population ?



# Is this intrinsic?... Let's learn from Neanderthal

Article

## The major genetic risk factor for severe COVID-19 is inherited from Neanderthals

<https://doi.org/10.1038/s41586-020-2818-3> Hugo Zeberg<sup>1,2</sup> & Svante Pääbo<sup>1,3</sup>



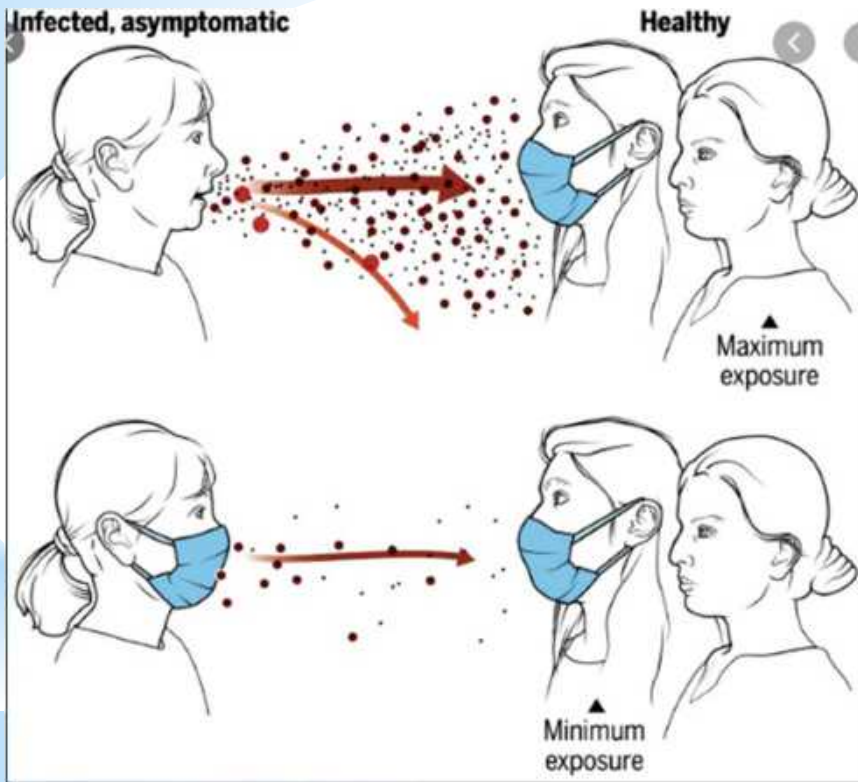
Fig. 3 | Geographical distribution of the Neanderthal core haplotype that confers risk for severe COVID-19.

# Enhanced stress experience DUE to restrictions



- ◆ How does **stress** help the virus ?
- ◆ *via* cortisol-mediated hyper-adaptation an impairment of the barrier function of the gut, site of the anti-inflammatory mucosal immunity
- ◆ leading to a **generalized inflammatory syndrome** with neuro—inflammation and consequent « sickness disease »
  - episodes of insomnia, depressive state, chronic fatigue syndrome...  
obsessional thoughts
  - mimicking **premature aging**

# FEAR is also limiting social interaction



- ◆ Talking AND laughing are already considered contamination friendly

## \* In summary...

1. Upon infection, immune over reaction could be linked to ***underlying stress***,
2. Health-measures (lock-down, mask-wearing) ***add to stress***,
3. Limited social contact, crucial for health, adds a ***supplementary layer of stress***.



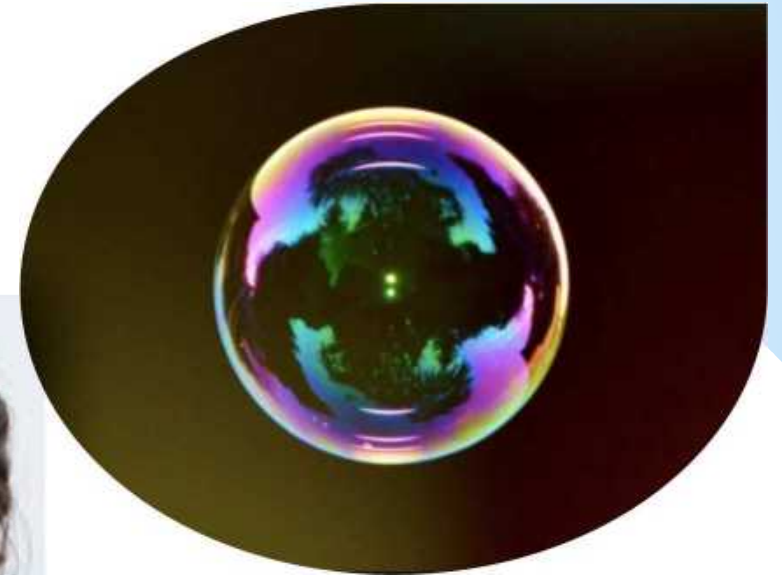


# Masks leave only ONE zone open to interaction

The *peri-orbital* area  
a strategic social contact zone



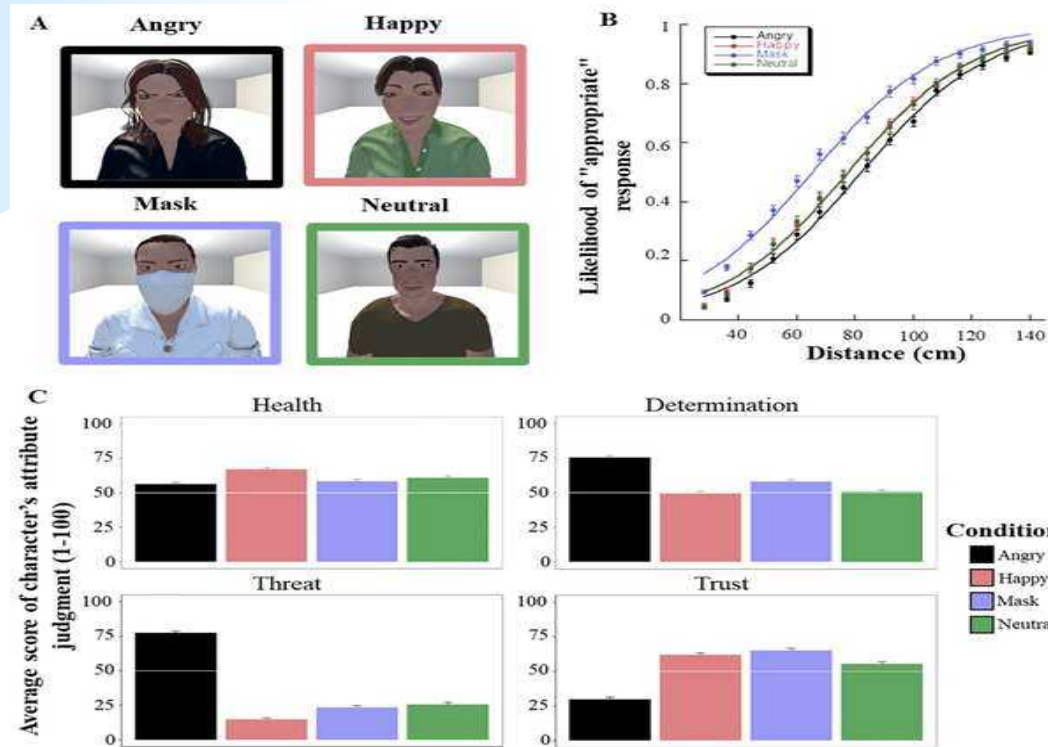
Elisabeth Vigée Le Brun auto portrait



# TOUCH and social grooming are replaced by EYE contact



# Stimuli judgments on interpersonal distancing (IPD)



1. Significant **decrease** in preferred IPD when confronted to a face mask in comparison to no mask.
2. The lesser the expected risk, the less social distancing.

Cartaud A, Quesque F, Coello Y (2020) Wearing a face mask against Covid-19 results in a reduction of social distancing. PLOS ONE 15(12): e0243023.  
<https://doi.org/10.1371/journal.pone.0243023>  
<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0243023>

# ANY neurocognitive consequences ?



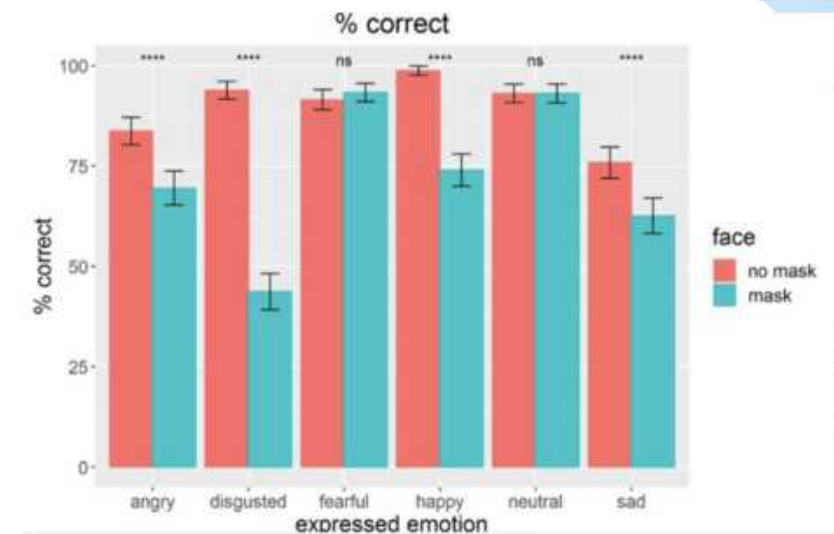
IPD (interpersonal distance) depends on the affective dimension of social interaction, affected by the current Covid-19 context

## ORIGINAL RESEARCH ARTICLE

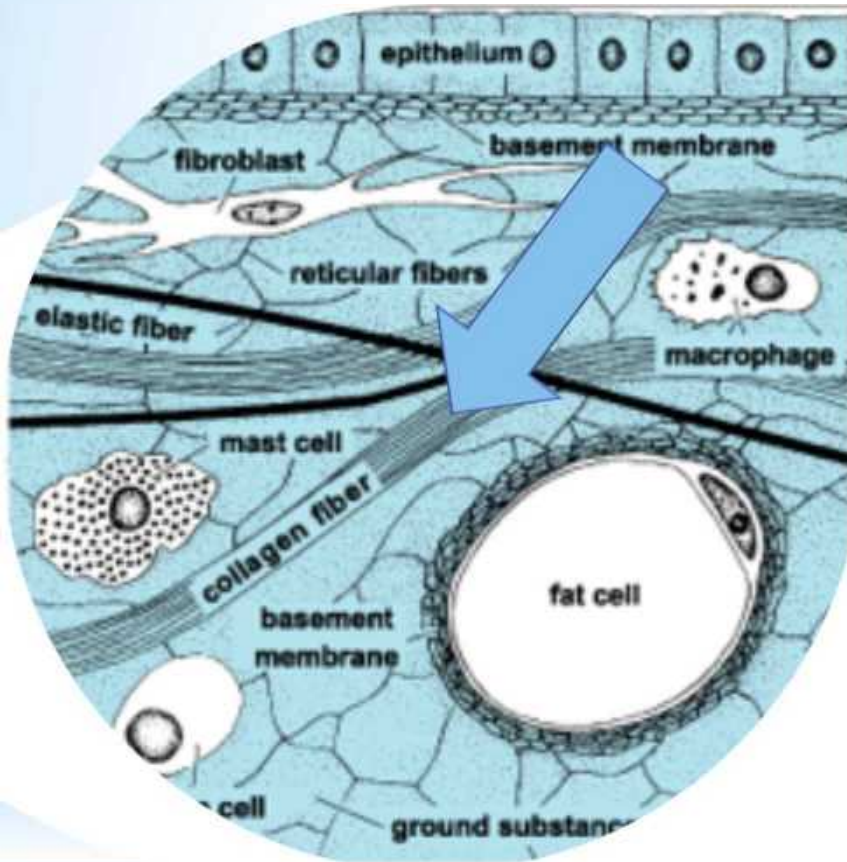
Front. Psychol., 25 September 2020 | <https://doi.org/10.3389/fpsyg.2020.566886>

## Wearing Face Masks Strongly Confuses Counterparts in Reading Emotions

Claus-Christian Carbon<sup>1,2\*</sup>



# What about COLLAGEN fibres?



Collagen fibers are empty pipes, which **convey fluids**, aqueous or in the form of gel, thus contributing to the transport of cerebrospinal fluid (CSF).

# Periorbital area: a FLEXIBLE zone between tension and relaxation

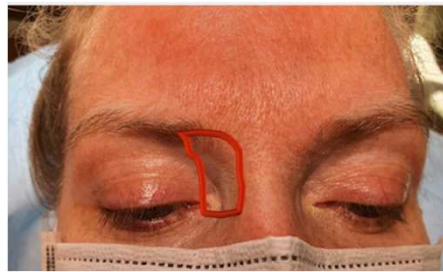
**Protocol** : clinostatism and topical treatment with monoterpen extract

- ◆ *tension* vs relaxation
- ◆ *hypoxia* vs better blood perfusion
- ◆ peri-nasal *edema* decrease

Stress

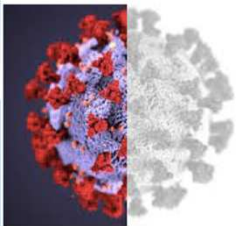
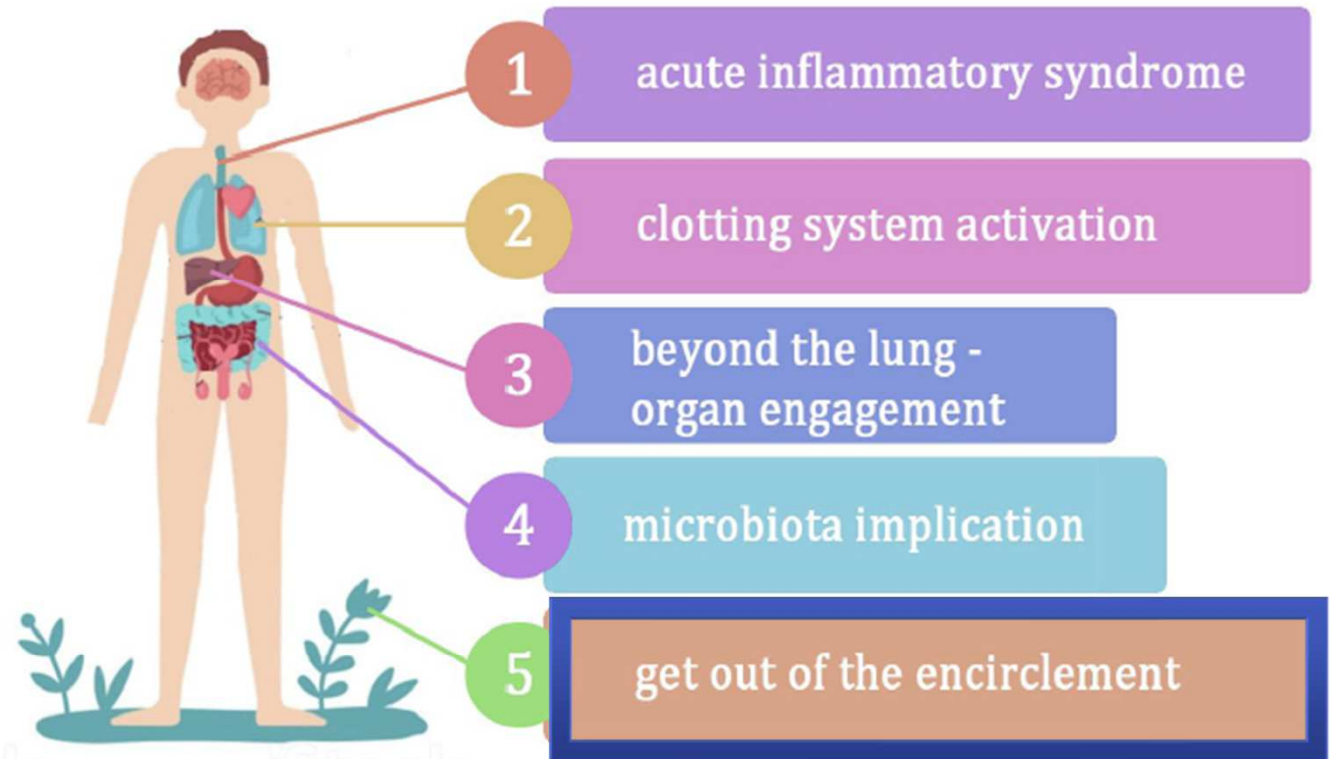


Relief



Images by Dr S Pariente, dermatologist Paris

# Let's step OUT of the encirclement



**SARS-COV-2 INFECTION  
HALLMARKS AND  
POSSIBLE REMEDIES**

Patrizia A d'ALESSIO MD PhD<sup>1</sup>

# and concentrate ON prevention of inflammation

## Barrier function restoration

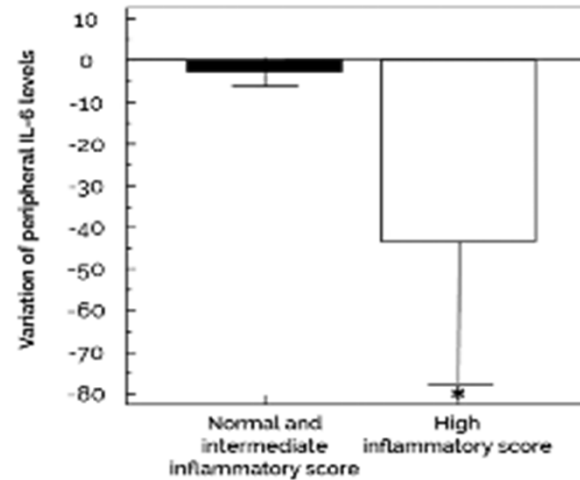
**Table 1**  
AISA: significant effect on strengthening the epithelial barrier function

	Control	AISA			
		75 $\mu$ M	150 $\mu$ M	750 $\mu$ M	1500 $\mu$ M
R <sup>t</sup>	107 $\pm$ 3%	106 $\pm$ 4%	112 $\pm$ 3%	132 $\pm$ 3%	153 $\pm$ 4%
n	9	6	6	6	6
p		n.s.	n.s.	<0.001	<0.001

Evaluation of the electrical resistance ( $\Omega \cdot \text{CM}^2$ )  
percentage of the initial resistance : Rt.

Life Sciences **2013**;92:1151-1156

## Anti-inflammatory effect



Clin Nutr. **2016**;35:812-818

**antioxidants**

Review  
**Terpenoids as Potential Geroprotectors**

Ekaterina Proshkina <sup>1</sup>, Sergey Plyusnin <sup>1,2</sup>, Tatyana Babak <sup>1</sup>, Ekaterina Lashmanova <sup>1</sup>, Faniya Maganova <sup>3</sup>, Liubov Koval <sup>1,2</sup>, Elena Platonova <sup>1,2</sup>, Mikhail Shaposhnikov <sup>1</sup> and Alexey Moskalev <sup>1,2,\*</sup>

Food and Chemical Toxicology 123 (2019) 233–257

Contents lists available at ScienceDirect

**Food and Chemical Toxicology**

journal homepage: [www.elsevier.com/locate/foodchemtox](http://www.elsevier.com/locate/foodchemtox)

Monoterpenes modulating cytokines - A review

Jullyana S.S. Quintans<sup>a</sup>, Saravanan Shanmugam<sup>a</sup>, Luana Heimfarth<sup>a</sup>, Adriano Antunes S. Araújo<sup>b</sup>, Jackson R.G.da S. Almeida<sup>c</sup>, Laurent Picot<sup>c</sup>, Lucindo J. Quintans-Júnior<sup>a,\*</sup>

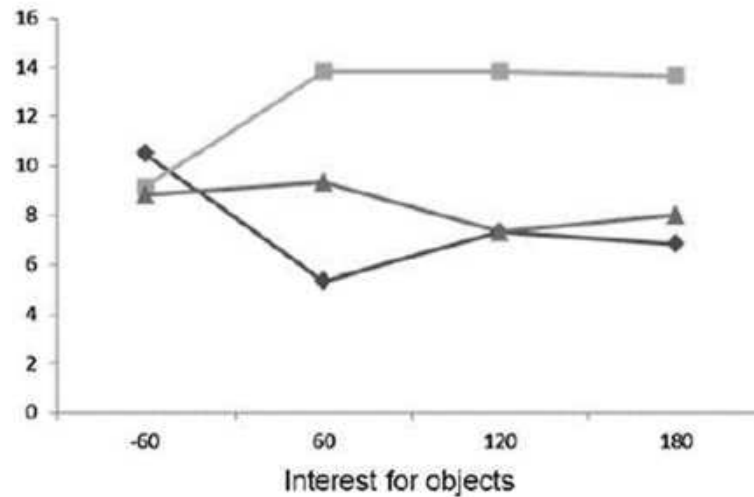
<sup>a</sup>Laboratory of Neuroscience and Pharmacological Assays, Department of Physiology, Federal University of Sergipe, São Cristóvão, Sergipe, Brazil  
<sup>b</sup>Department of Pharmacy (DFA), Federal University of Sergipe, São Cristóvão, SE, Brazil  
<sup>c</sup>Center for Studies and Research of Medicinal Plants (CERPLAME), Federal University of San Francisco Valley (UNIVASF), Petrolina, Pernambuco, Brazil  
<sup>\*</sup>UMR CNRS 7246 LUNEX, University of La Rochelle, 17042, La Rochelle, France





# We can get rid of the pandemic STRESS effect!

## Motivational effect



Rejuvenation Res. 2014;17:145-149

## Mood modulation effect

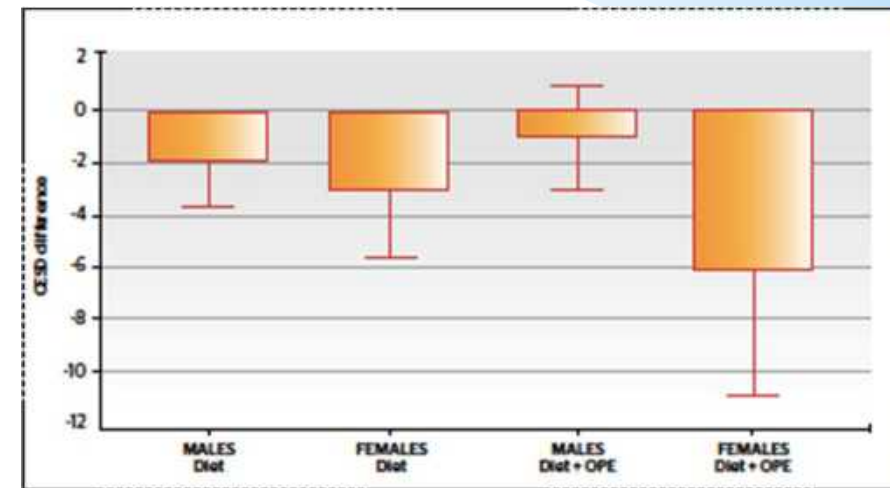


Figure 3 Gender partition and CES-D variation in diet versus diet plus OPE.

PRIME 2012;July/August:30-37



# Pragmatic interventions?



# Will we ever recover the positive effect of gentle touch enhancing *body awareness*?

Mindfulness and vagal activation indeed allows to escape from **immune thunderstorm**

Promotion of self-esteem strategies provide major shielding against different **sources of stress**



Emma Thompson & husband

Currently, at least work on the periorbital area...



rejuvenating effect,  
sustained by *glance*  
quality,

moving from sad  
and depressed to  
sparkling and  
smiling...

Thank you for your attention  
**Credits & Questions ?!**



Comprendre le monde,  
construire l'avenir



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