



26 Feb 2022



COVID e malattie infettive stagionali

COVID 19 e danni al SNC : Focus sulle Patologie Neurodegenerative

*Giuseppe Neri Neurologo e Psichiatra
Past-President SNO , Società Neurologi Ospedalieri*



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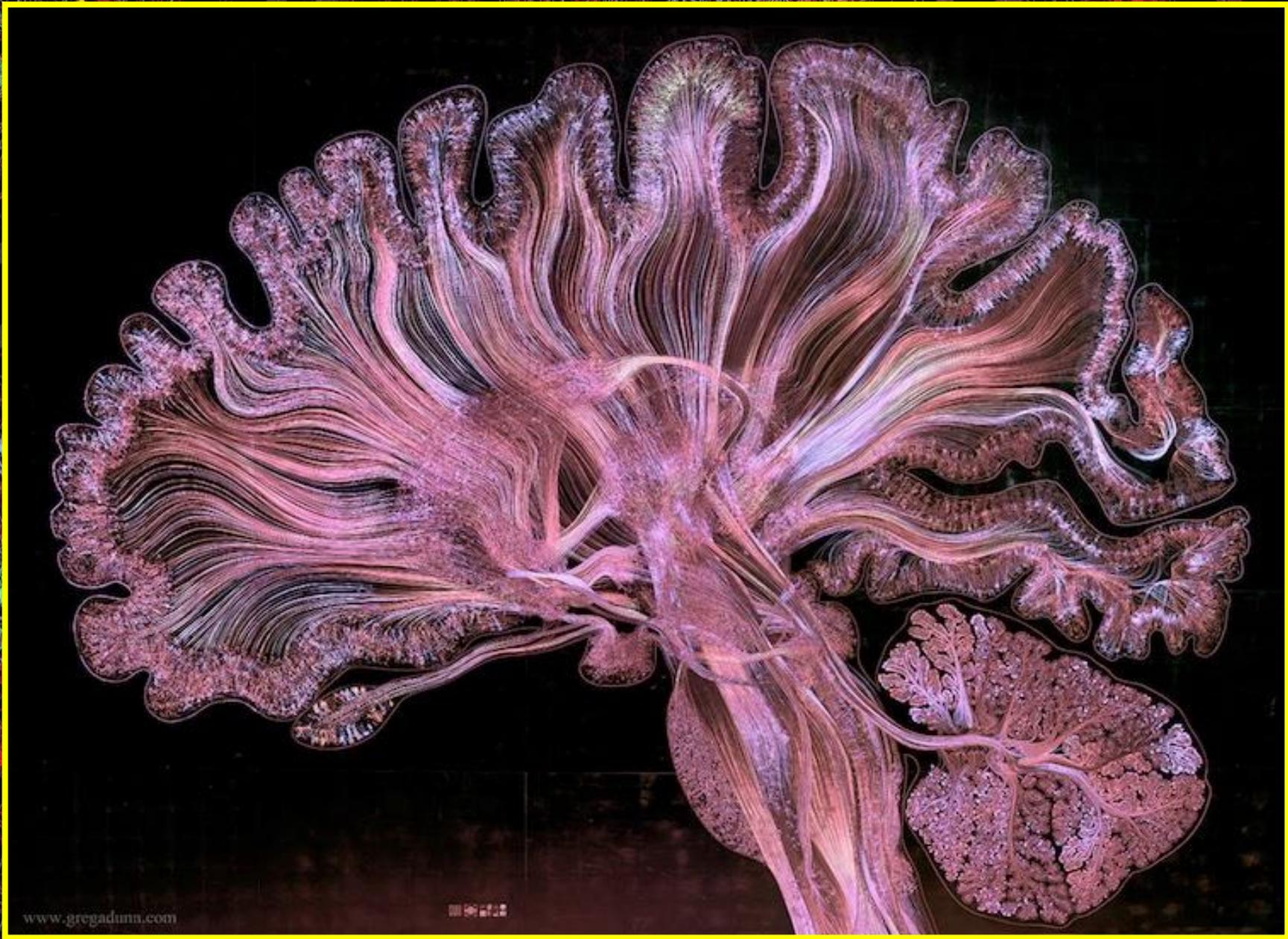
**THE BRAIN: AN UNEXPECTED
TARGET OF COVID-19**

NEUROTOXICITY AS AN EMERGING
HEALTH OUTCOME OF COVID-19

May 12, 2021 .



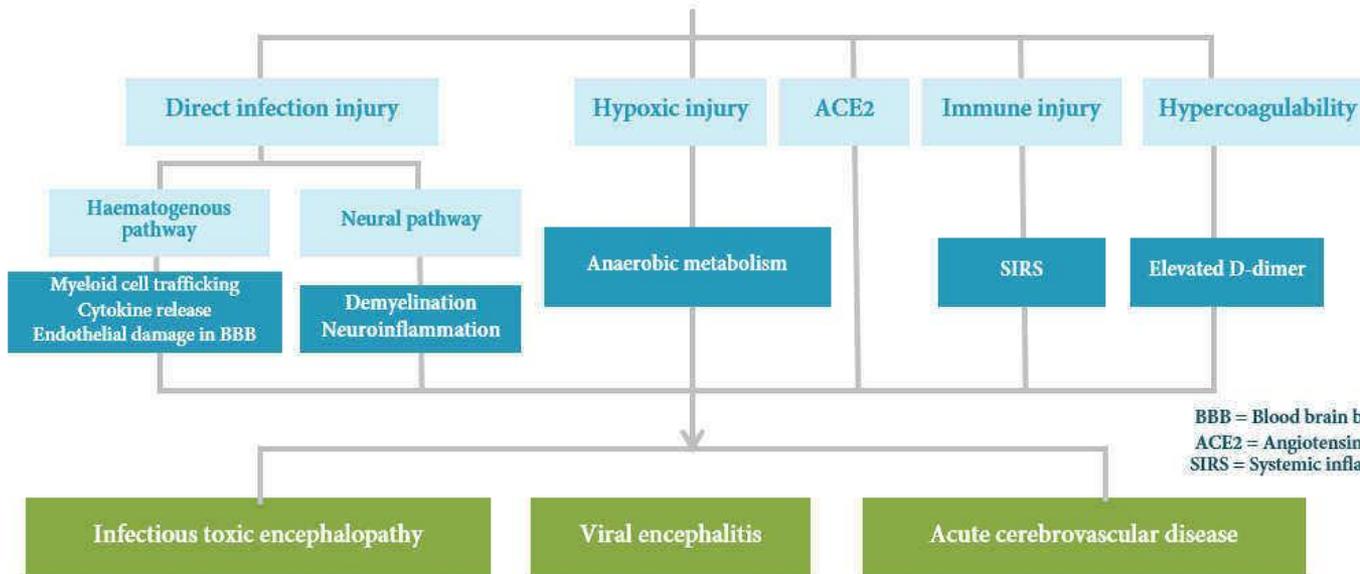
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Pathophysiology of CNS Involvement with SARS-CoV-2



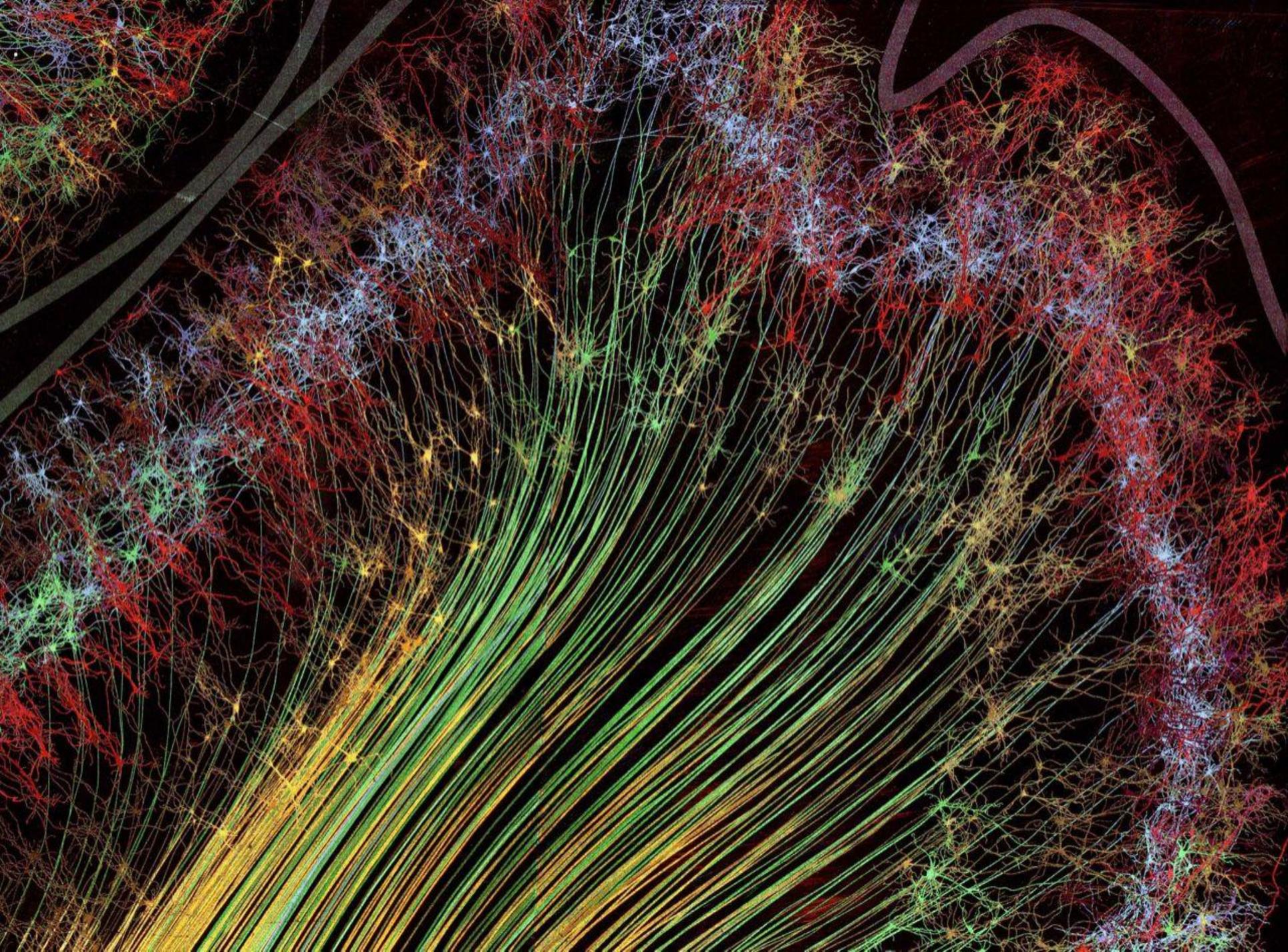
SARS-CoV-2 INVASION

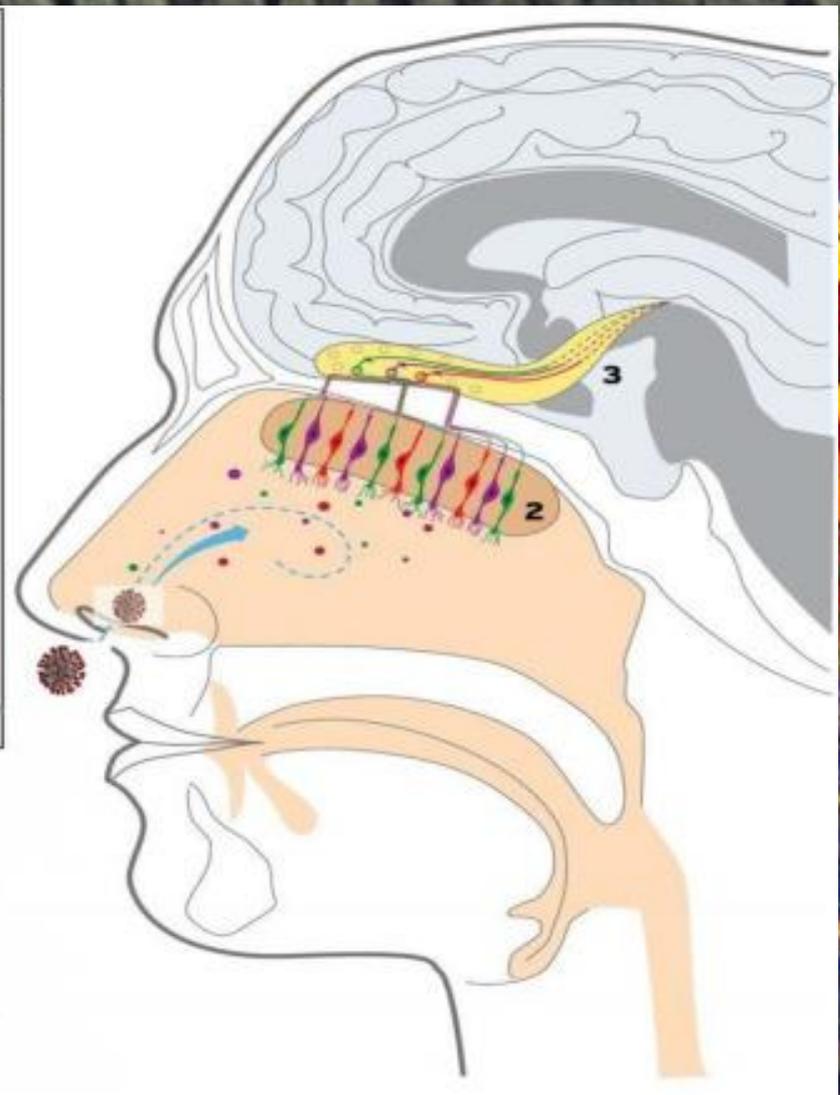
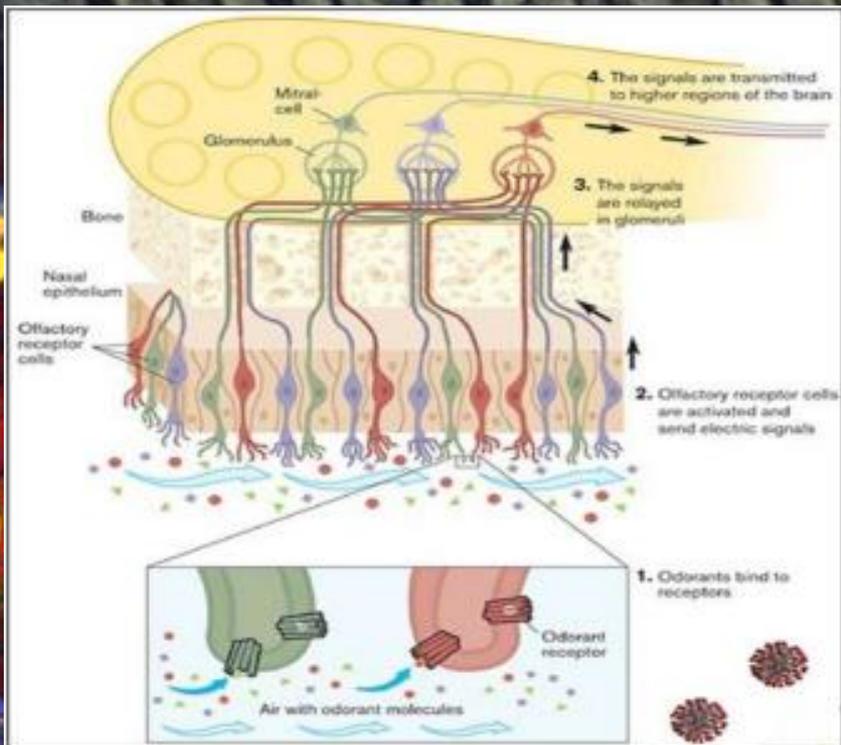


BBB = Blood brain barrier
ACE2 = Angiotensin-converting enzyme 2
SIRS = Systemic inflammatory response syndrome

Adapted and modified from Wu, Y., Xu, X., Chen, Z., Duan, J., Hashimoto, K., Yang, L., ... & Yang, C. (2020). Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain, Behavior, and Immunity*.

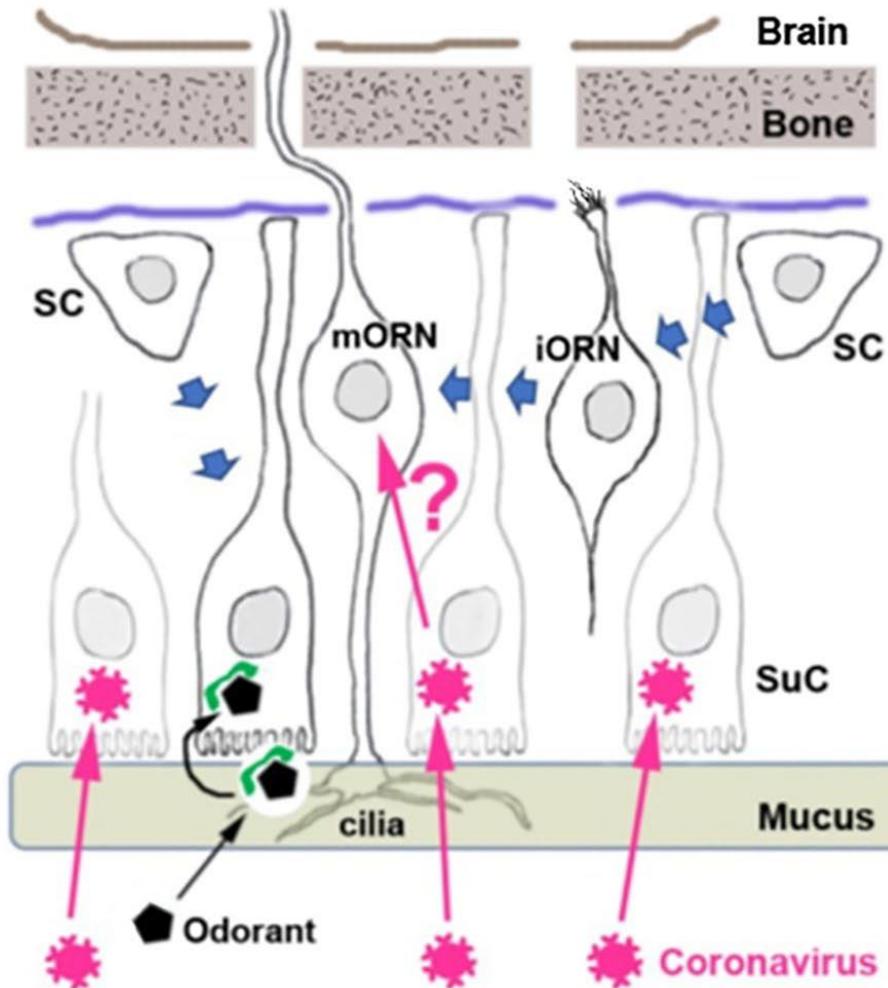






COVID-19





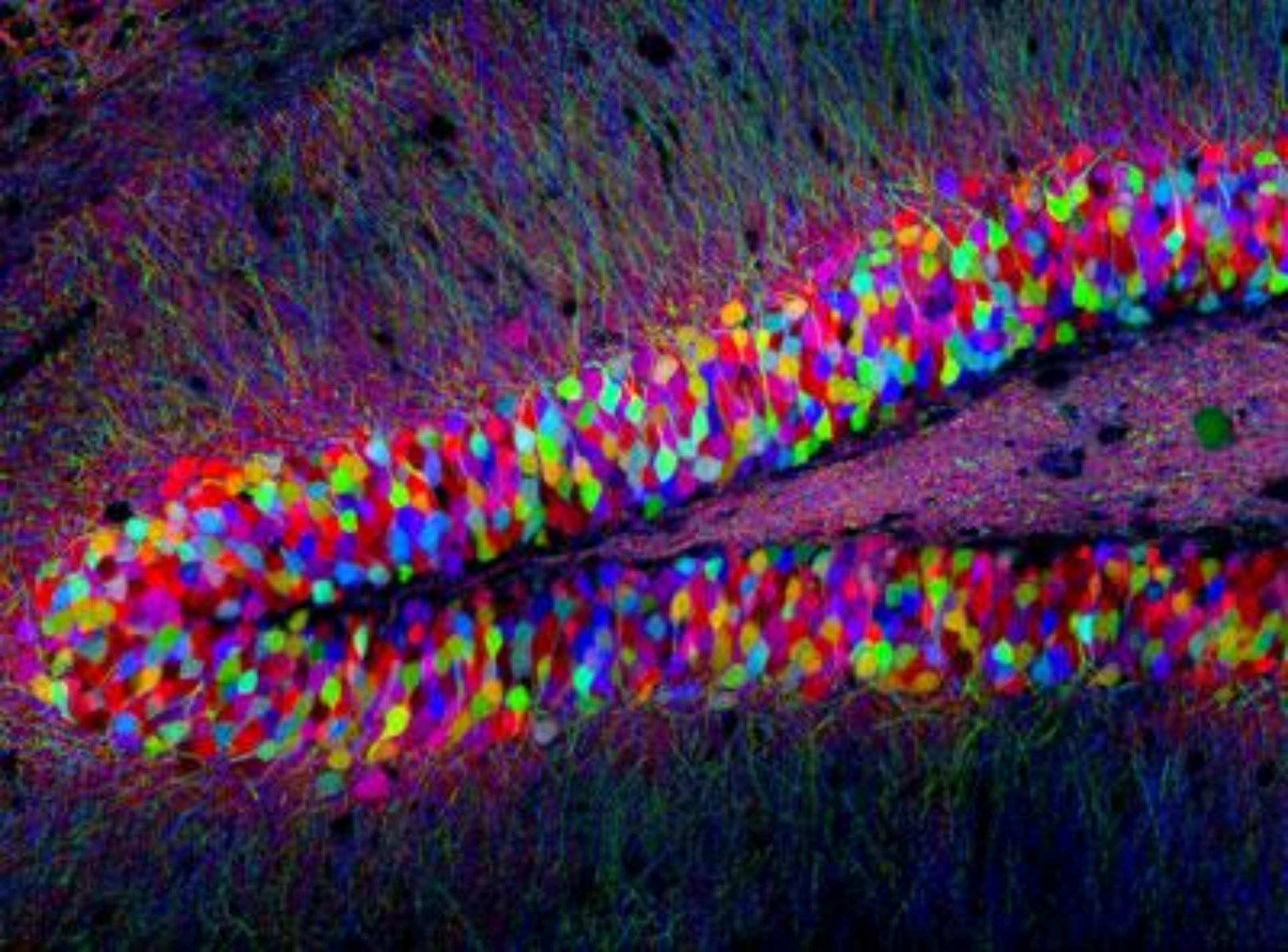
Stem Cells (SC) rapidly regenerate SuCs damaged by the virus

Stem Cells (SC) regenerate ORNs, but with a slow time course

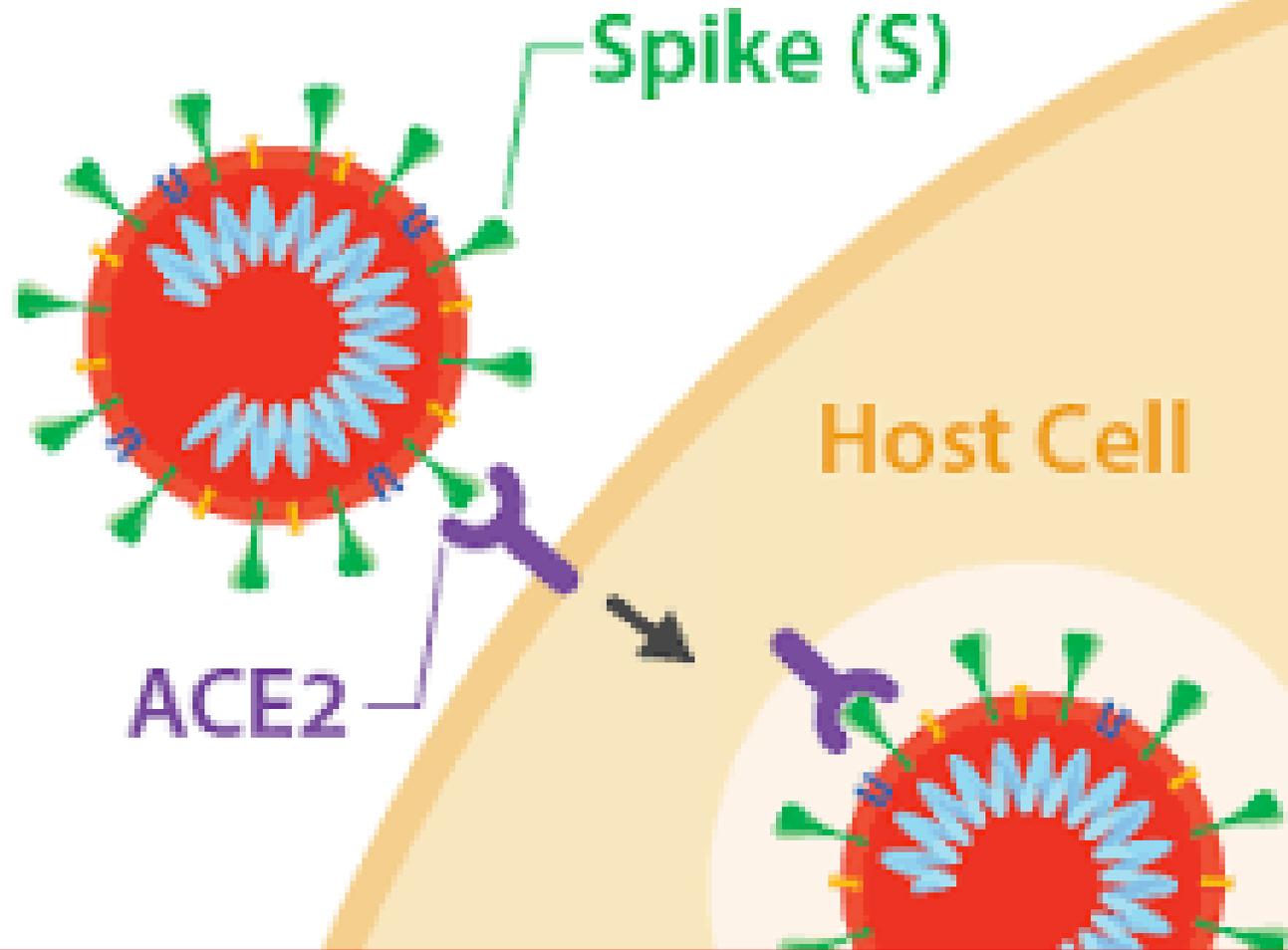
SuCs assist ORNs with odorant processing and help to maintain the cilia of ORNs

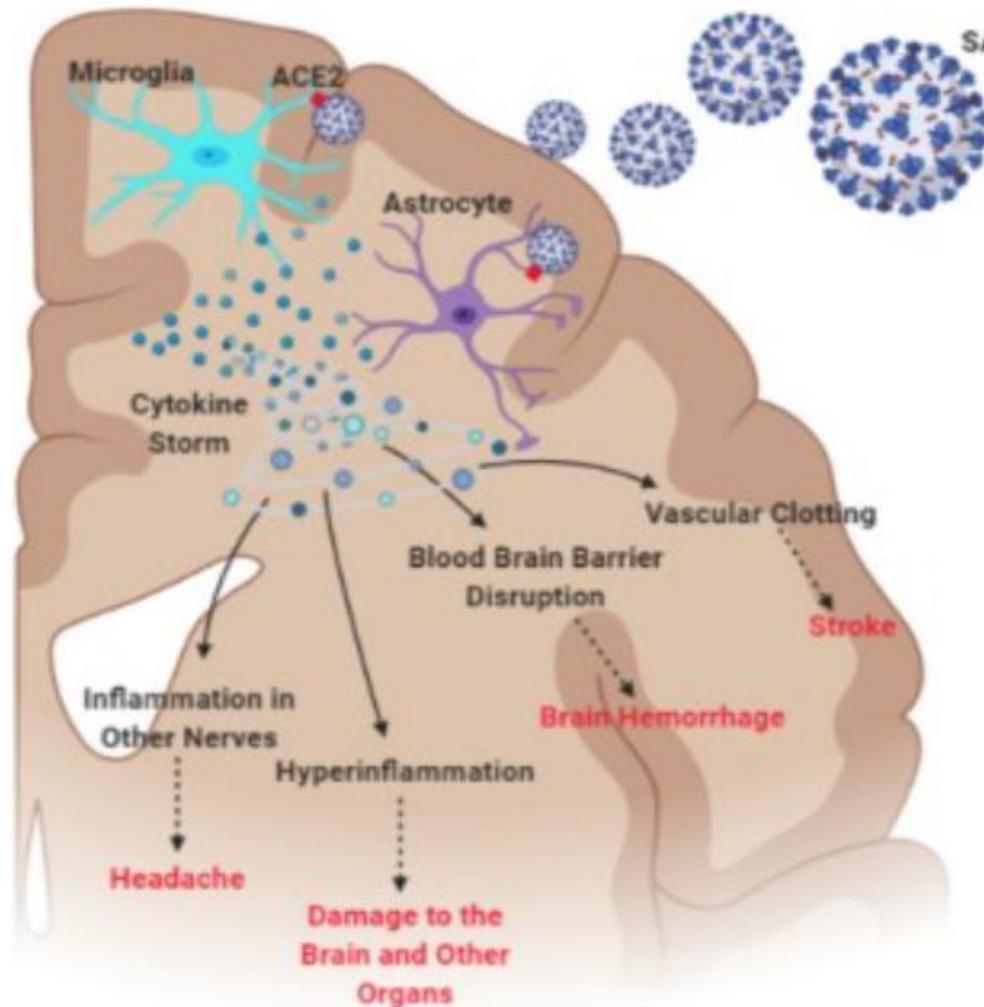
It is not yet known whether the virus can transfer from SuCs to ORNs.

The virus infects SuCs, because they express the virus entry proteins, ACE2 and TMPRSS2, causing death of SuCs



SARS-CoV-2





1. SARS-CoV-2 binds to ACE2 receptors on microglia and astrocytes.

2. This initiates an increase in cytokines.

3. An overexpression of cytokines leads to a "cytokine storm" that contributes to patients' neurological symptoms.

4. These lead to the underlying mechanisms of the patient's symptomology .

Figure 3: Neuroinflammatory mechanism(s) of SARS-CoV-2-induced neurological effects in the brain.



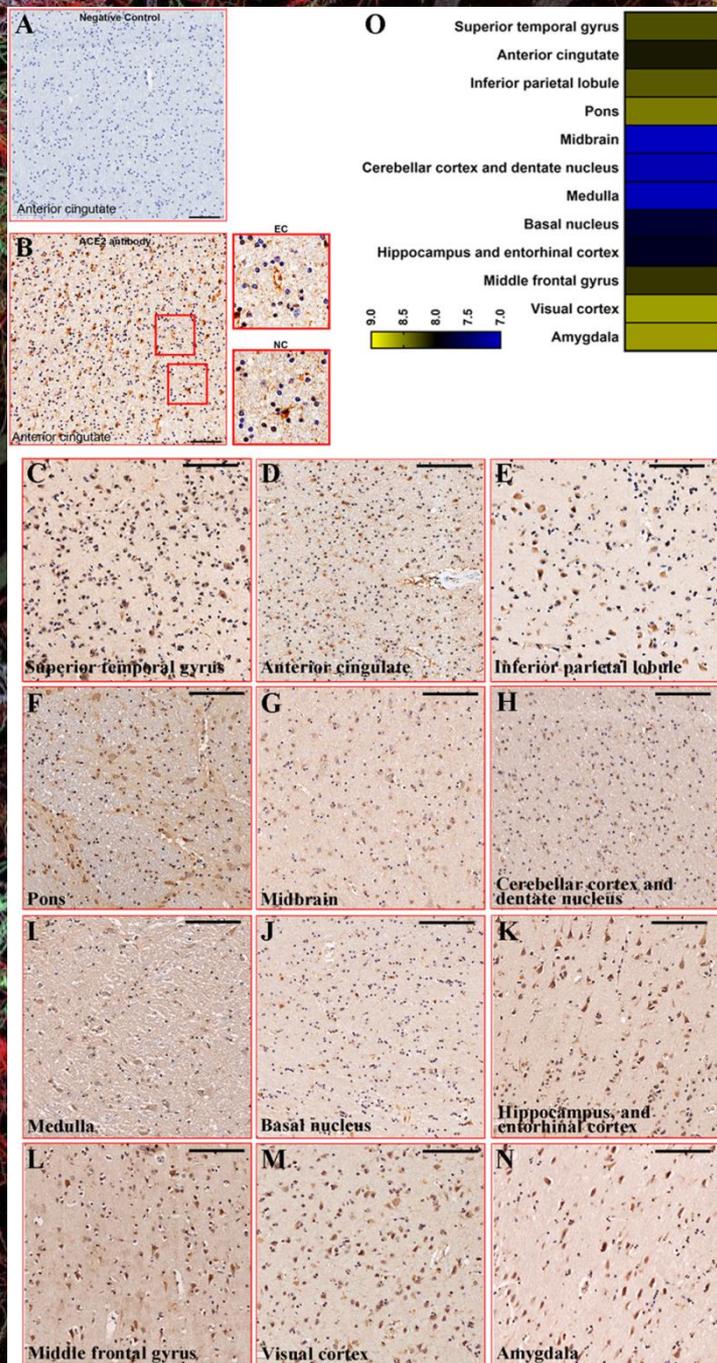


FIGURE 2 | Representative images of ACE2 expression among brain regions. (A) Immunostaining of negative control for ACE2 in the anterior cingulate cortex (PTB270). Scale bar = 100 mm. (B) Immunostaining of ACE2 by Rabbit anti-ACE2 antibody in the anterior cingulate cortex (PTB270). Scale bar = 100 mm. The enlarged views were listed on the right. EC, endothelial cell; NC, non-vascular cell. (C–N) Representative images of ACE2 expression among brain regions in health control. Scale bar = 100 mm. (O)

Huan Cui^{1†}, Si Su^{1†}, Yan Cao^{1†}, Chao Ma^{1,2*} and Wenying Qiu^{1*}

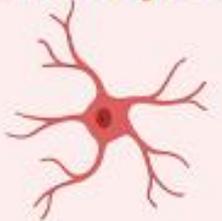
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published : 25 June 2021
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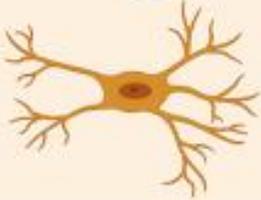
a **Neurons**



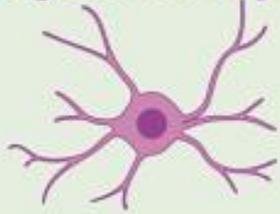
Astrocytes



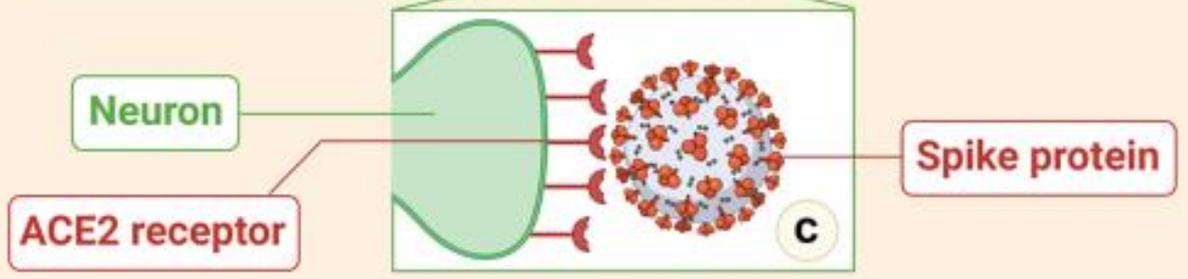
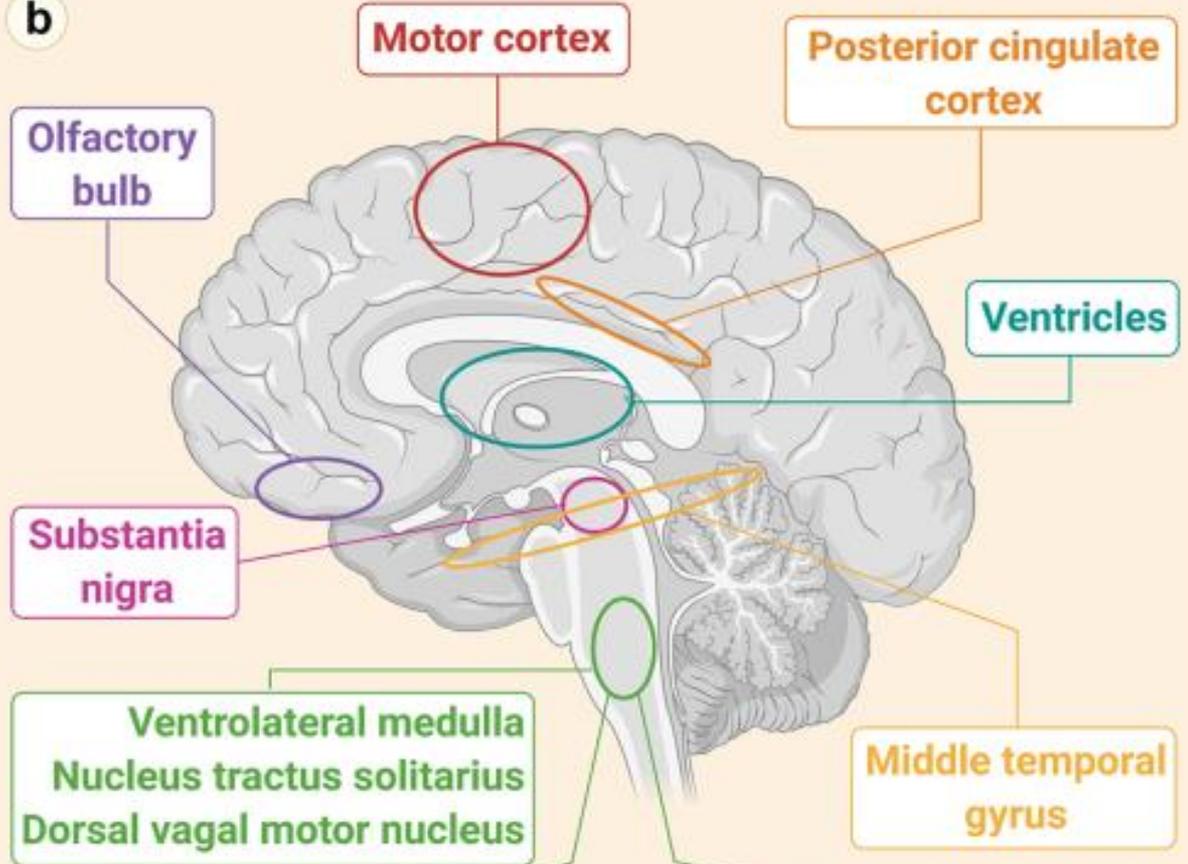
Microglia

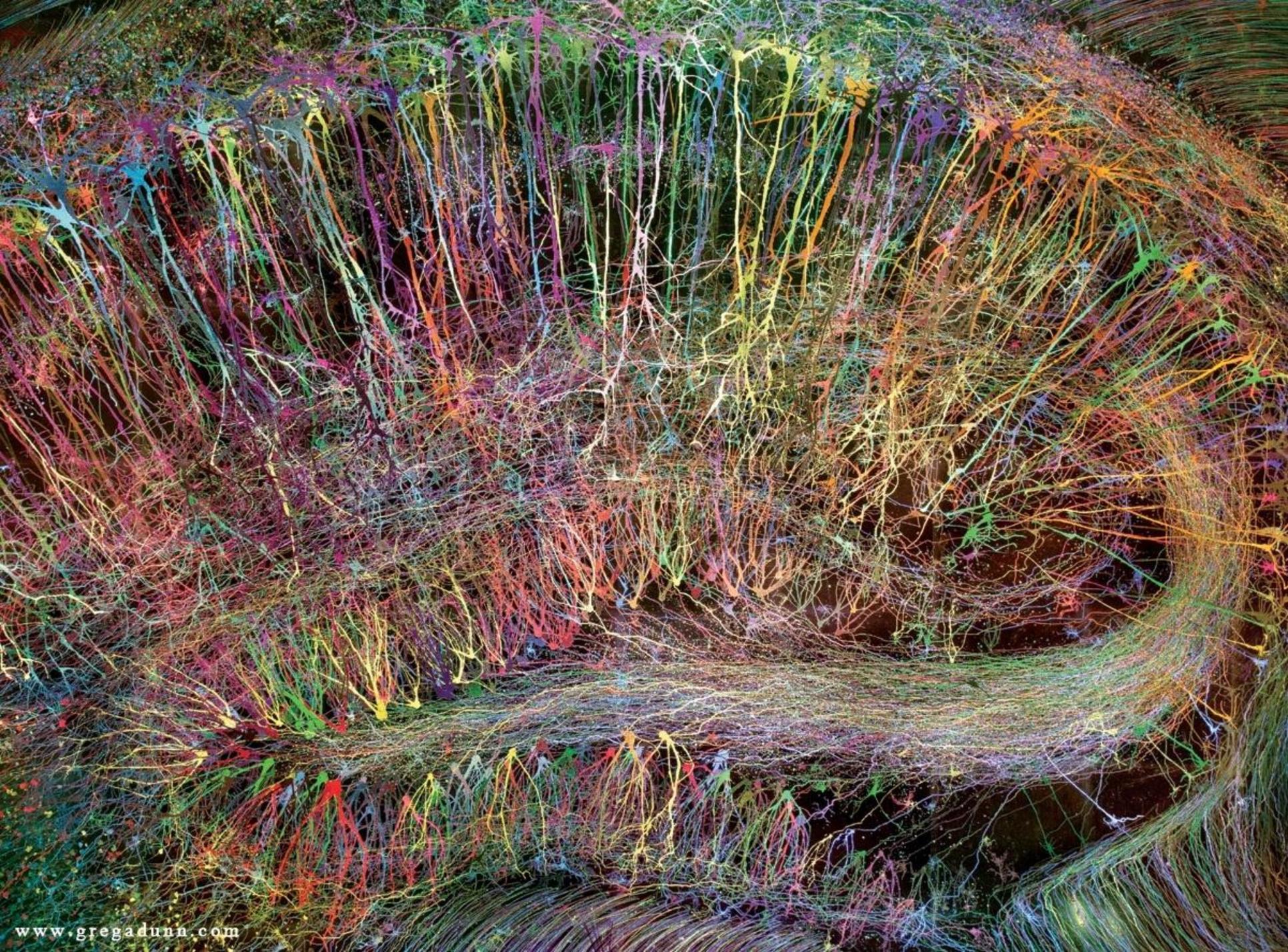


Oligodendrocytes



b





Trends in Neurosciences

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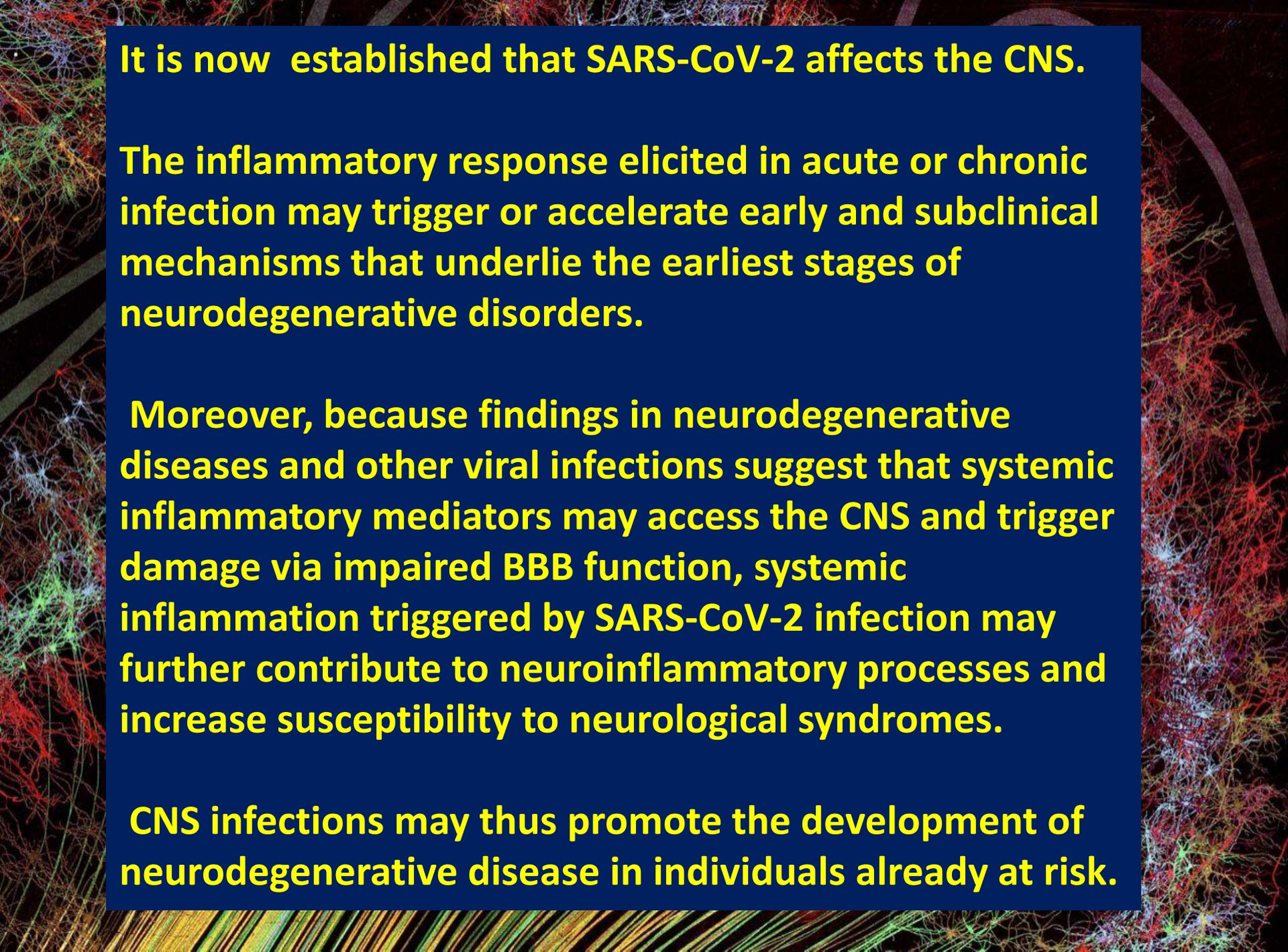
Science & Society

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and the Central Nervous System

Fernanda G. De Felice^{1, 2, 3}  , Fernanda Tovar-Moll^{4, 5}, Jorge Moll⁵, Douglas P. Munoz², Sergio T. Ferreira^{1, 6}

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- ² Centre for Neuroscience Studies, Queen's University, Kingston, ON K7L 3N6, Canada
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- ⁶ Institute of Biophysics Carlos Chagas Filho, Federal University of Rio de Janeiro, Rio de Janeiro, RJ 21941-902, Brazil

Available online 21 April 2020, Version of Record 26 May 2020.

A microscopic image of neural tissue, likely a brain section, showing a dense network of neurons and axons. The tissue is stained with red and green dyes, highlighting specific cellular components. The background is dark, making the stained structures stand out. The text is overlaid on a blue rectangular area in the center of the image.

It is now established that SARS-CoV-2 affects the CNS.

The inflammatory response elicited in acute or chronic infection may trigger or accelerate early and subclinical mechanisms that underlie the earliest stages of neurodegenerative disorders.

Moreover, because findings in neurodegenerative diseases and other viral infections suggest that systemic inflammatory mediators may access the CNS and trigger damage via impaired BBB function, systemic inflammation triggered by SARS-CoV-2 infection may further contribute to neuroinflammatory processes and increase susceptibility to neurological syndromes.

CNS infections may thus promote the development of neurodegenerative disease in individuals already at risk.



**SEGNI e SINTOMI
NEUROLOGICI e/o PSICHIATRICI
Sono presenti nel 94 % dei casi clinici di
Covid**

**L'interessamento diretto del S N C è
dimostrato in oltre il 50% dei casi**

<i>Neurological Symptom</i>	<i>Proposed Mechanism</i>	<i>Acute or Chronic</i>	<i>Population of Patients</i>
Headache	Neuroinflammation	Both	12%
Anosmia (Loss of Smell)	Neuroinflammation or Nerve Damage	Both	50-60%
Ageusia (Loss of Taste)	Neuroinflammation or Nerve Damage	Both	40%
Confusion - "Brain Fog"	Neuroinflammation or Low Oxygen	Both	30-80%
Stroke	Neuroinflammation or Low Oxygen	More Chronic	1.8-2%
Brain Hemorrhage	Neuroinflammation	More Chronic	up to 12%
Memory Loss	Follows Stroke or HPA axis alteration	Both	27-34%
Psychiatric Disorder	Neuroinflammation, HPA axis alteration, unknown	More Chronic	5-8%
Fever	Inflammation	More Acute	80%



**L'altra faccia della realtà della
Pandemia COVID – Sars 2**

Per molti decenni intorno al Neurologo è stata confezionata una immagine il cui connotato distintivo era dato da :

- ELEVATA ERUDIZIONE
- RAFFINATE ED APPROFONDITE COMPETENZE SCIENTIFICO-CLINICHE
- ELEGANTE E COMPLETO BAGAGLIO DI SEMEIOLOGIA CLINICA

a queste caratteristiche risultava **INDISSOLUBILMENTE** legata, non senza la attiva collaborazione dei Neurologi stessi, l'immagine di disporre di **RISORSE TERAPEUTICHE INCISIVE MOLTO LIMITATE.**

La conclusione spesso tratta dai Colleghi di altre discipline, dalle Direzioni Sanitarie e dalle Direzioni Generali, dagli Assessorati alla Sanità , dai decisori politici era :

**“ IL NEUROLOGO E' UN SOFISTICATO
POSSESSORE DI ELABORATI SISTEMI
DI CATEGORIZZAZIONE NOSOGRAFICA...
ma NON CURA EFFICACEMENTE E NON GUARISCE
SE NON UNA ESIGUA MINORANZA DEI PAZIENTI CHE TRATTA “**



**La Neurologie..c'est une
discipline contemplative.
Démerdez-vous avec ça .**

Daniel Pennac

Des Chrétiens et des Mores, 1996



DANIEL PENNAC
**Ultime notizie
dalla famiglia**

UNIVERSALE
ECONOMICA
FELTRINELLI

JLB





**Dopo inizio pandemia il tempo medio di arrivo
in Ospedale dei pazienti con
Accidente Cerebrovascolare acuto
è passato da 96 a 176 minuti
rispetto all'esordio dei sintomi**

**Nello studio policentrico SNO sulle
Neurologie Ospedaliere
la incidenza della S. di Guillain- Barré
è aumentata , dall'esordio della pandemia,
del 300 %**

Stroke care in Italy: An overview of strategies to manage acute stroke in COVID-19 time

European Stroke Journal
2020, Vol. 5(3) 222–229
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2020
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DOI: 10.1177/2396987320942622
journals.sagepub.com/home/eso



Marialuisa Zedde¹ , Francesca Romana Pezzella²,
Maurizio Paciaroni³, Francesco Corea⁴, Nicoletta Reale⁵,
Danilo Toni⁶ and Valeria Caso³

Abstract

Purpose: To analyse structural and non-structural modifications of acute stroke care pathways undertaken at health-care institutions across the regions of Italy due to the coronavirus disease 2019 (COVID-19) pandemic.

Methods: Research on National decrees specific for the pandemic was carried out. The stroke pathways of four Italian regions from North to South, such as Lombardy, Veneto, Lazio and Campania, were analysed before and after the pandemic outbreak.

Findings: On 29 February 2020, the Italian Minister of Health issued national guidelines on how to address the COVID-19 emergency. Stroke management was affected and required changes, basically resulting in the need to prioritise the ongoing COVID-19 emergency. In the most affected regions, the closure of departments and hospitals led to a complete reorganisation of previously functioning stroke networks. With the closure of several Stroke Units and Stroke Centres, the transportation time to hospital lengthened significantly, especially for the outlying populations.

Discussion: The COVID-19 pandemic outbreak has been spreading rapidly in Italy and placing an overwhelming burden on healthcare systems. In response to this, political and healthcare decision-makers worked together to develop and implement efforts to sustain the national healthcare system while fighting the pandemic. Stroke care pathways changed during the pandemic and different organisational models were applied in the most affected regions.

Conclusions: Stroke treatment pathways will need to be redesigned so to guarantee that severe and acute disease patients do not lose their rights to the access and delivery of care during the COVID-19 pandemics.

Keywords

Stroke, stroke management, COVID-19, pandemic, Italy

Date received: 30 April 2020; accepted: 18 June 2020

**ACCESSI IN PRONTO SOCCORSO per
ACCIDENTE CEREBROVASCOLARE ACUTO
da Marzo 2020 in avanti**

- 57,5 % = 112.452 pazienti
non trattati o trattati non adeguatamente

RITARDO NELL'ARRIVO in P.S. degli ICTUS : da 90 a 180 minuti
PAZIENTI ELIGIBILI AL TRATTAMENTO TROMBOLITICO : - 34 %
TROMBOLISI Endovenose per ICTUS : - 26 %
TROMBECTOMIE ENDOVASCOLARI ARTERIOSE PRIMARIE : - 41 %

MORTALITA' PER ACCIDENTI CEREBROVASCOLARI ACUTI

**MORTALITA' INTRA-OSPEDALIERA : + 22 %
MORTALITA' a 30 GIORNI : + 31 %**

**MORTI POTENZIALMENTE EVITABILI
PER ICTUS da MARZO 2020 :**

**ECCESSO MORTI epoca POST COVID : INTRA-OSPEDALE : 9178
ECCESSO MORTI epoca POST-COVID COVID : A 30 GIORNI : 1012**

**Dal 1 MARZO 2020 , data convenzionale di inizio
della PANDEMIA COVID in ITALIA**

**Abbiamo perso 9178 persone in più
per accidenti cerebrovascolari acuti
rispetto a Marzo- Novembre 2019**

**502 morti per ictus in più ogni mese ,
32 al mese in più nella area di Roma Capitale**

**E' ragionevole presumere che almeno altri 7000 pazienti siano deceduti a
casa non essendo mai stati portati , causa Covid, in Ospedale**

Life
isn't about waiting
for the storm to pass...
It's learning to



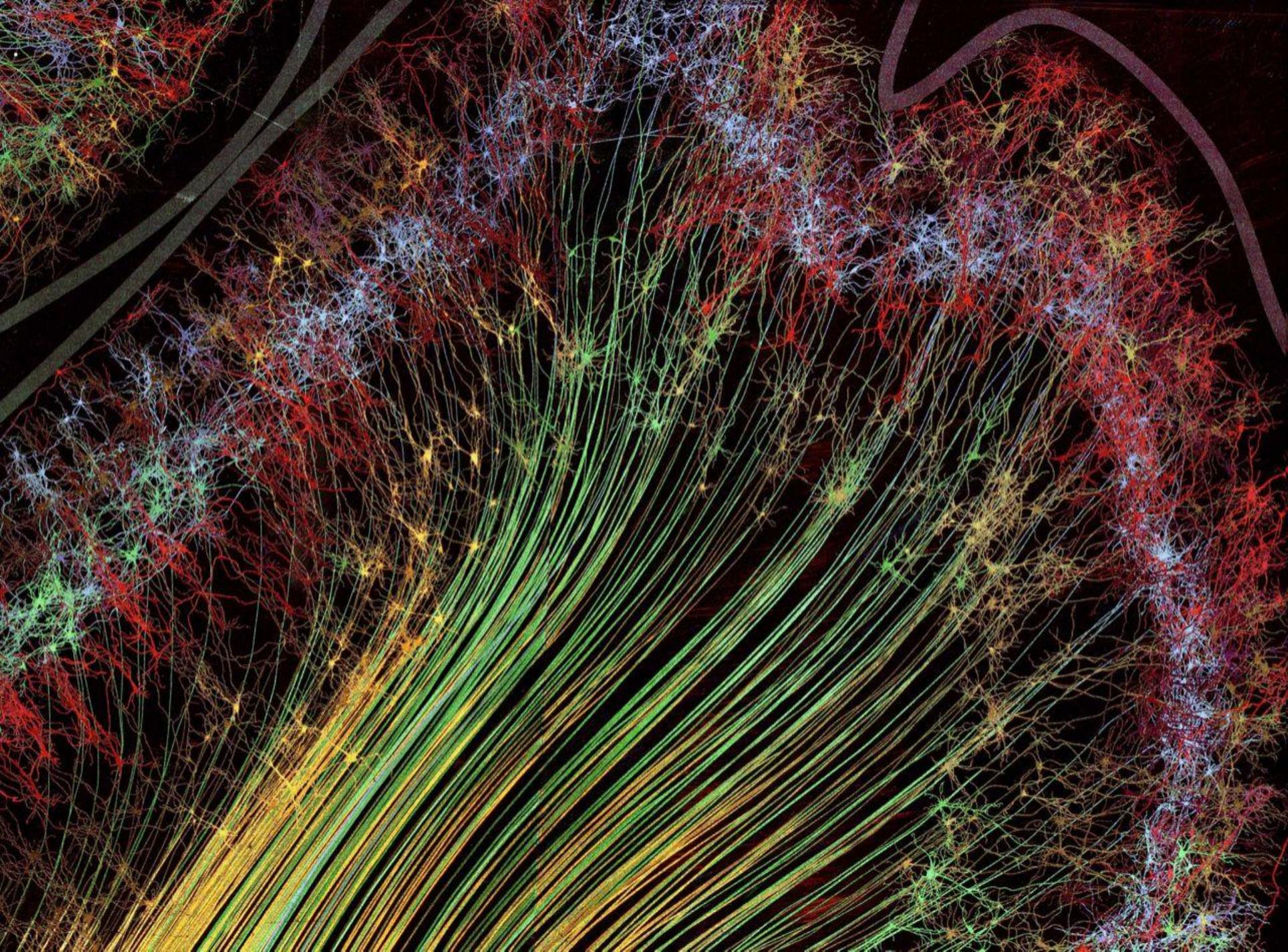
dance in the rain

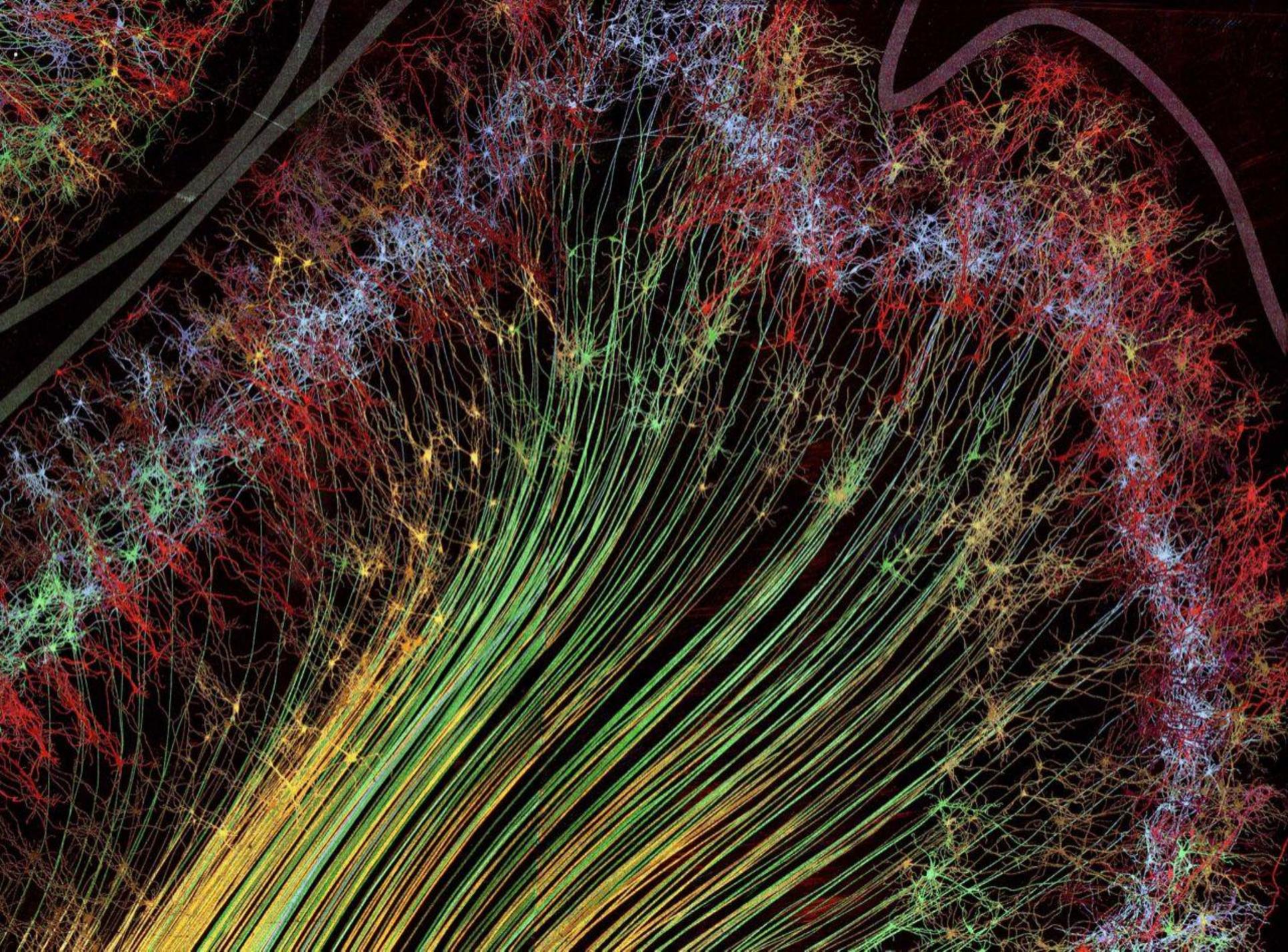
DANCE UNDER THE RAIN

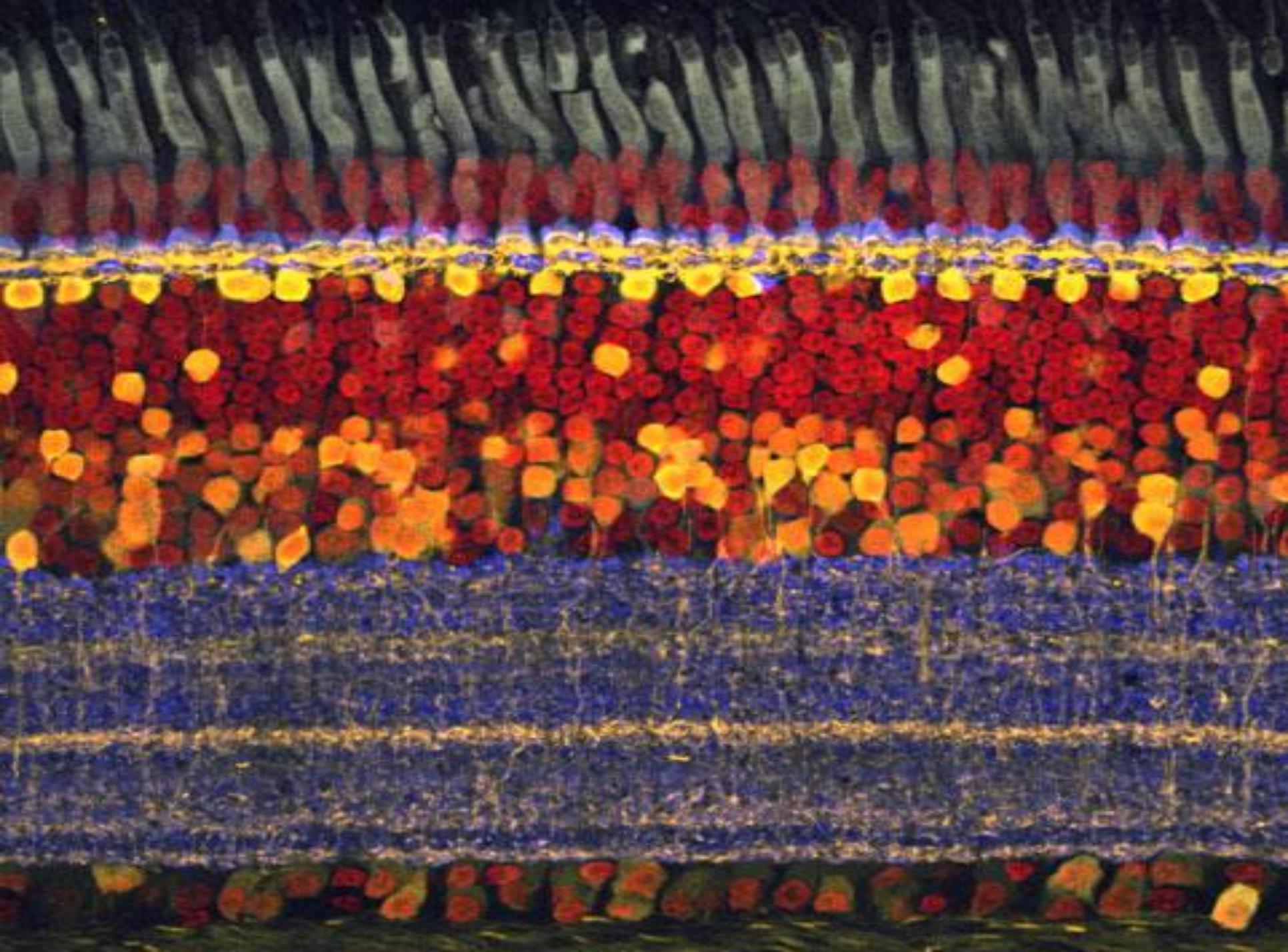


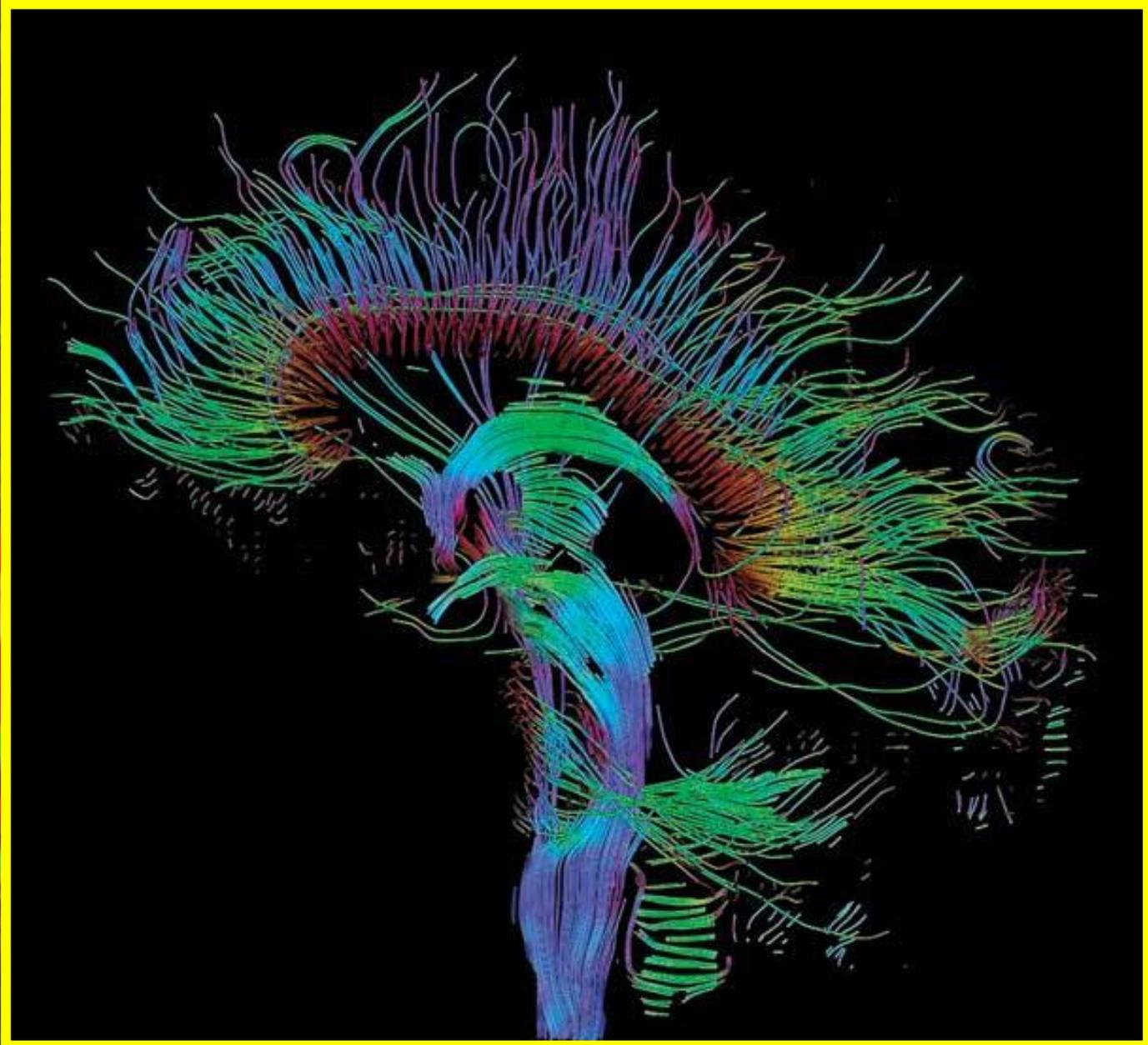
**UCRAINA
LIBERA !**

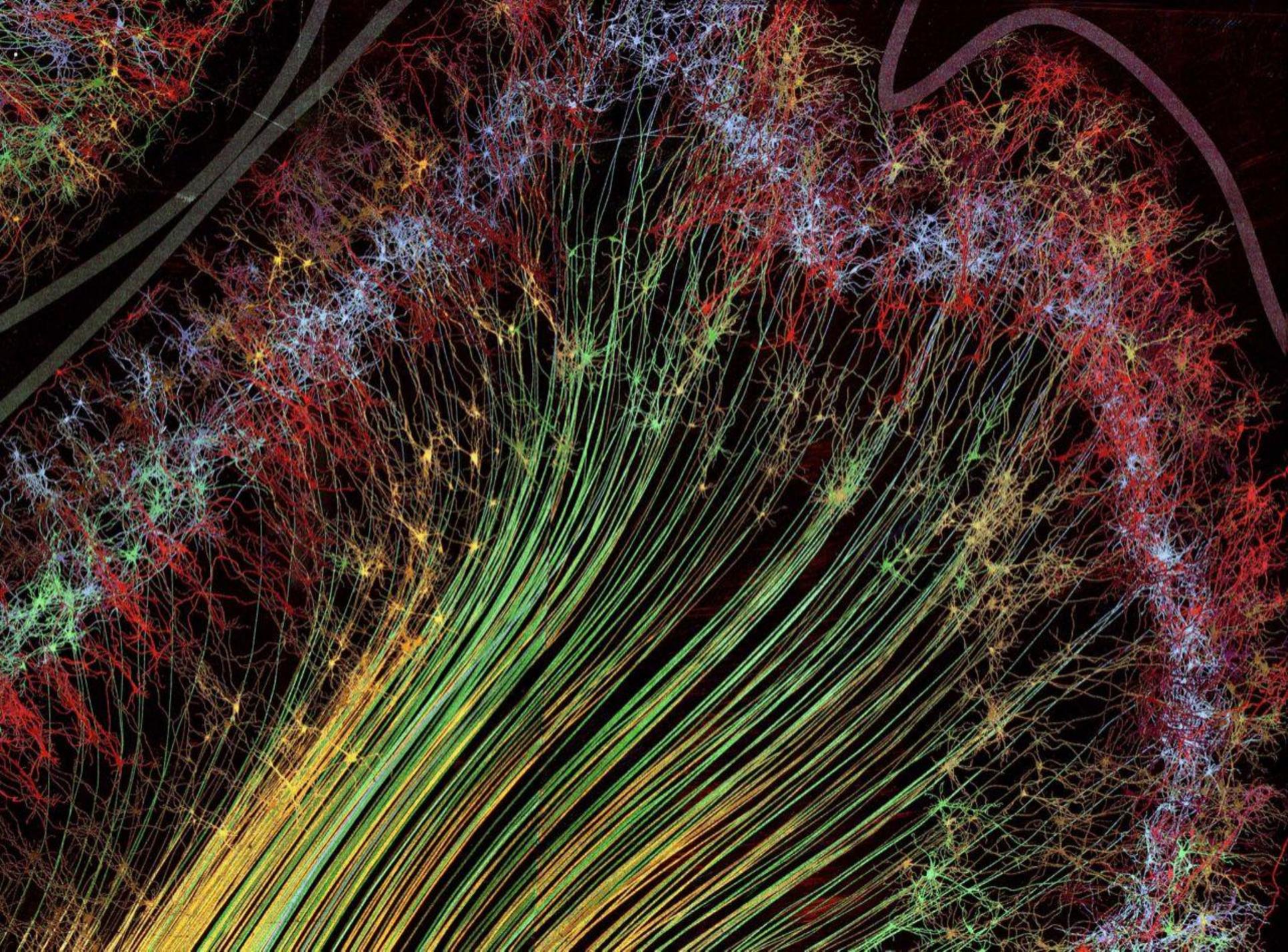












INFEZIONI del S. N. C.

Infezioni del sistema nervoso centrale

- **Meningite** → processo infiammatorio con interessamento delle leptomeningi
- **Encefalite** → processo infiammatorio con interessamento del parenchima cerebrale
- **meningoencefalite** → processo infiammatorio con interessamento delle leptomeningi e del parenchima cerebrale
- **Encefalomyelite** → infezione del parenchima cerebrale e del midollo spinale
- **Ascesso cerebrale** → infezione focale (occupante spazio)

**Interessamento del SISTEMA NERVOSO Centrale e Periferico
in corso di INFEZIONI da AGENTI TRASMISSIBILI**

BATTERI

VIRUS

Agenti Trasmissibili Non Convenzionali



P R I O N I

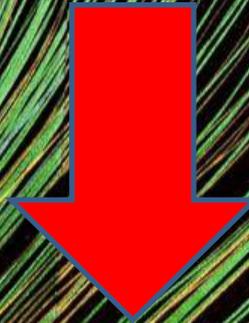
Encefalopatie Spongiose Subacute Trasmmissibili

Malattia di Creutzfeldt – Jakob

New-Variant-CJD da  B S E (c.d. "Mucca Pazza)

**RETE delle NEUROLOGIE
OSPEDALIERE OSPEDALIERE
ROMANE**

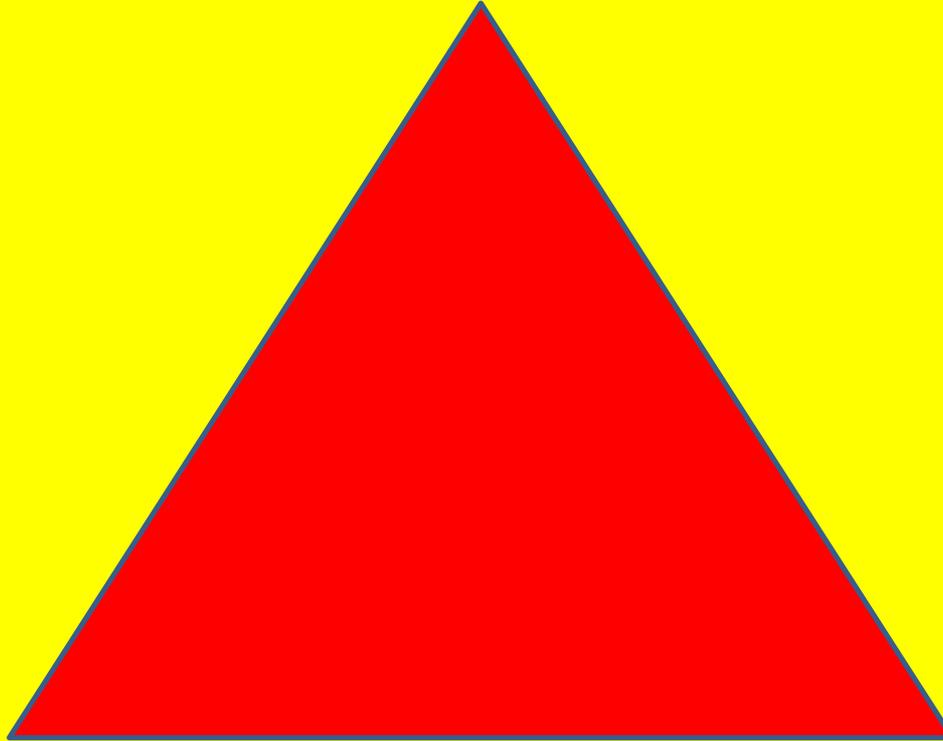
**SAN CAMILLO
SAN FILIPPO**



SPALLANZANI

SAN FILIPPO NERI

Prof. Alberto EDERLI



SAN CAMILLO

Prof. Giovanni ALEMA'

SPALLANZANI

Prof. Giuseppe VISCO



JOURNAL ARTICLE

The AIDS Dementia Complex

Richard W. Price and Bruce J. Brew

The Journal of Infectious Diseases

Vol. 158, No. 5 (Nov., 1988), pp. 1079-1083 (5 pages)

Published By: Oxford University Press

<https://www.jstor.org/stable/30136610>

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Abstract

Note from Dr. Merle A. Sande - Progressive dementia has been recognized as a complication of human immunodeficiency virus infection almost since the beginning of the epidemic. To many infectious diseases clinicians, however, the AIDS dementia complex remains ambiguous, and the clinical approach to this problem is less clearly defined than that for other infection-associated syndromes. Dr. Richard W. Price and his colleagues at Memorial Sloan Kettering Cancer Center have, to a large extent, been responsible for defining this entity. In this AIDS Commentary they present their views of the current state of knowledge regarding the etiology, clinical presentation, and diagnostic and therapeutic approaches to the AIDS dementia complex.



ORIGINAL RESEARCH

Guillain-Barré syndrome and COVID-19: an observational multicentre study from two Italian hotspot regions

Massimiliano Filosto ¹, Stefano Cotti Piccinelli ², Stefano Gazzina,³ Camillo Foresti,⁴ Barbara Frigeni,⁴ Maria Cristina Servalli,⁴ Maria Sessa,⁴ Giuseppe Cosentino,⁵ Enrico Marchioni,⁶ Sabrina Ravaglia,⁵ Chiara Briani ⁷, Francesca Castellani,⁷ Gabriella Zara,⁷ Francesca Bianchi,⁸ Ubaldo Del Carro,⁸ Raffaella Fazio,⁸ Massimo Filippi ⁸, Eugenio Magni,⁹ Giuseppe Natalini,¹⁰ Francesco Palmerini,⁹ Anna Maria Perotti,⁹ Andrea Bellomo,¹¹ Maurizio Osio,¹² Giuseppe Scopelliti ¹¹, Marinella Carpo,¹³ Andrea Rasera,¹⁴ Giovanna Squintani,¹⁴ Pietro Emiliano Doneddu,¹⁵ Valeria Bertasi,¹⁶ Maria Sofia Cotelli,¹⁶ Laura Bertolasi,¹⁷ Gian Maria Fabrizi ¹⁷, Sergio Ferrari ¹⁷, Federico Ranieri ¹⁷, Francesca Caprioli,¹⁸ Elena Grappa,¹⁹ Laura Broglio,³ Giovanni De Maria,³ Ugo Leggio,³ Loris Poli,²⁰ Frank Rasulo,²¹ Nicola Latronico,²¹ Eduardo Nobile-Orazio ¹⁵, Alessandro Padovani,² Antonino Uncini ²²

► Additional material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/jnnp-2020-324837>).

For numbered affiliations see end of article.

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Prof. Massimiliano Filosto, Department of Clinical and Experimental Sciences, University of Brescia; Unit of Neurology, ASST Spedali Civili; NeMO-Brescia Clinical Center for Neuromuscular Diseases, Brescia, Italy; massimiliano.filosto@unibs.it

AP and AU contributed equally to the study and share senior authorship.

Received 14 August 2020
Revised 17 October 2020
Accepted 17 October 2020

ABSTRACT

Objective Single cases and small series of Guillain-Barré syndrome (GBS) have been reported during the SARS-CoV-2 outbreak worldwide. We evaluated incidence and clinical features of GBS in a cohort of patients from two regions of northern Italy with the highest number of patients with COVID-19.

Methods GBS cases diagnosed in 12 referral hospitals from Lombardy and Veneto in March and April 2020 were retrospectively collected. As a control population, GBS diagnosed in March and April 2019 in the same hospitals were considered.

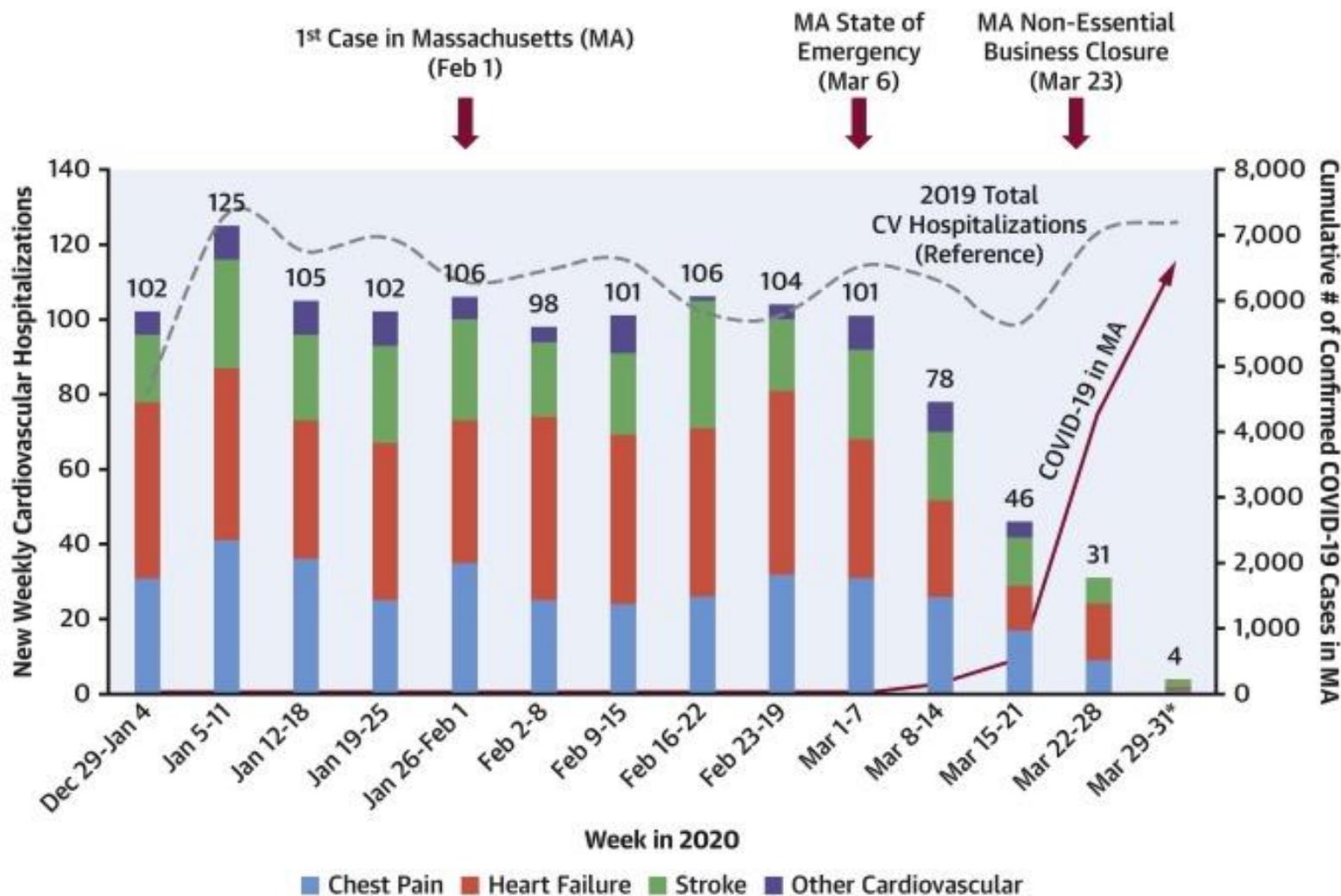
Results Incidence of GBS in March and April 2020 was 0.202/100 000/month (estimated rate 2.43/100 000/year) vs 0.077/100 000/month (estimated rate 0.93/100 000/year) in the same months of 2019 with a 2.6-fold increase. Estimated incidence of GBS in COVID-19-positive patients was 47.9/100 000 and in the COVID-19-positive hospitalised patients was 236/100 000. COVID-19-positive patients with GBS, when compared with COVID-19-negative subjects, showed lower MRC sum score (26.3+18.3 vs 41.4+14.8.

INTRODUCTION

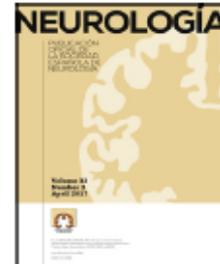
In December 2019, Wuhan in China became the centre of an outbreak of pneumonia caused by a novel coronavirus named SARS-CoV-2.¹ COVID-19 rapidly spread all over the world, acquiring the characteristics of a pandemic, and since February 2020, it has been spreading in Italy, particularly in the Lombardy and Veneto regions.² With the increasing understanding of the disease, many non-pulmonary symptoms were recognised, including neurological complications such as acute cerebrovascular diseases, seizures, meningitis, encephalitis and skeletal muscle involvement.^{3–5} From 1 April to 30 June 2020, 42 patients with SARS-CoV-2 infection and Guillain-Barré syndrome (GBS) have been reported mostly from Europe, and the number of cases is increasing weekly, suggesting a possible association.⁶

Nowadays, GBS is considered a diagnostic umbrella including a number of related autoimmune polyneuropathies classified in variants and subtypes.^{7,8} On the basis of electrophysiological

CENTRAL ILLUSTRATION: Changes in the Rate of Cause-Specific Cardiovascular Hospitalization During the COVID-19 Pandemic

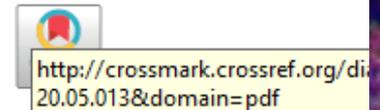


Bhatt, A.S. et al. J Am Coll Cardiol. 2020;76(3):280-8.



ORIGINAL ARTICLE

Impact of the COVID-19 pandemic on the organisation of stroke care. Madrid Stroke Care Plan[☆]



B. Fuentes^{a,*}, M. Alonso de Leciñana^a, P. Calleja-Castaño^b, J. Carneado-Ruiz^c, J. Egido-Herrero^d, A. Gil-Núñez^e, J. Masjuán-Vallejo^f, J. Vivancos-Mora^g, J. Rodríguez-Pardo^a, N. Riera-López^h, Á. Ximénez-Carrillo^g, A. Cruz-Culebras^f, C. Gómez-Escalonilla^d, E. Díez-Tejedor^a, on behalf of the hospitals participating in the Madrid Stroke Care Plan

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^g Servicio de Neurología, Hospital Universitario de La Princesa, Universidad Autónoma de Madrid, Madrid, Spain

^h Servicio de Urgencias Médicas de Madrid, SUMMA-112, Madrid, Spain

2018

REGIONS	POPULATION	IVT centers	IVT treatments	EVT centers	EVT treatments
Liguria	1,575,000	10	571	2	191
Friuli VG	1,223,000	3	426	2	88
Alto Adige	511,750	1	172	1	76
Trentino	534,405	1	161	1	2
Abruzzo	1,328,000	7	401	4	87
Veneto	4,925,000	22 (22)	1,485	6 (6)	360
Tuscany	3,753,000	22	1,129	3	395
Emilia Romagna	4,451,000	14 (12)	1,264	5 (5)	585
Marche	1,551,000	7	365	1	82
Umbria	894,762	5	221	2	49
Piedmont	4,424,000	24	1,091	5	343
Sardinia	1,663,000	3	381	3	135
Lombardy	10,000,000	38 (8)	1,805	8 (6)	843
Lazio	5,882,000	20 (20)	1,049	7 (7)	476
Valle d'Aosta	128,298	1	20	1	14
Calabria	1,973,000	5	307	3	96
Sicily	5,082,000	17	696	3	163
Puglia	4,087,000	9	526	4	191
Basilicata	574,782	2	43	0	0
Campania	5,869,000	8 (8)	356	2 (2)	167
Molise	314,725	1	0	0	0
Totale	60,744,722	220	12,469	63	4,343

Attuali positivi

690.323

Incremento
-6.204

Dimessi / Guariti

1.052.163

Incremento
24.169

Deceduti

63.387

Incremento
761

Totale casi

1.805.873

Incremento
18.727

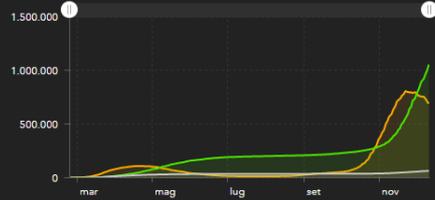
Dati Andamento

Dati Andamento

Dati Andamento

Dati Andamento

Andamento nazionale



Nuovi positivi



Positivi Variazione



Regioni - attuali positivi

Province - casi totali



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 Scheda metadati RNDI: dati - area
 Temi del dataset: Salute umana e sicurezza (Inspire) - ISO 19115: Salute
 Dati forniti dal Ministero della Salute
 Elaborazione e gestione dati e cura del Dipartimento della Protezione Civile

Download schede e dati:
 - Scheda nappilogo PDF
 - Dati CSV / JSON
 - Shape area
 - Metadata

Altri dati e informazioni

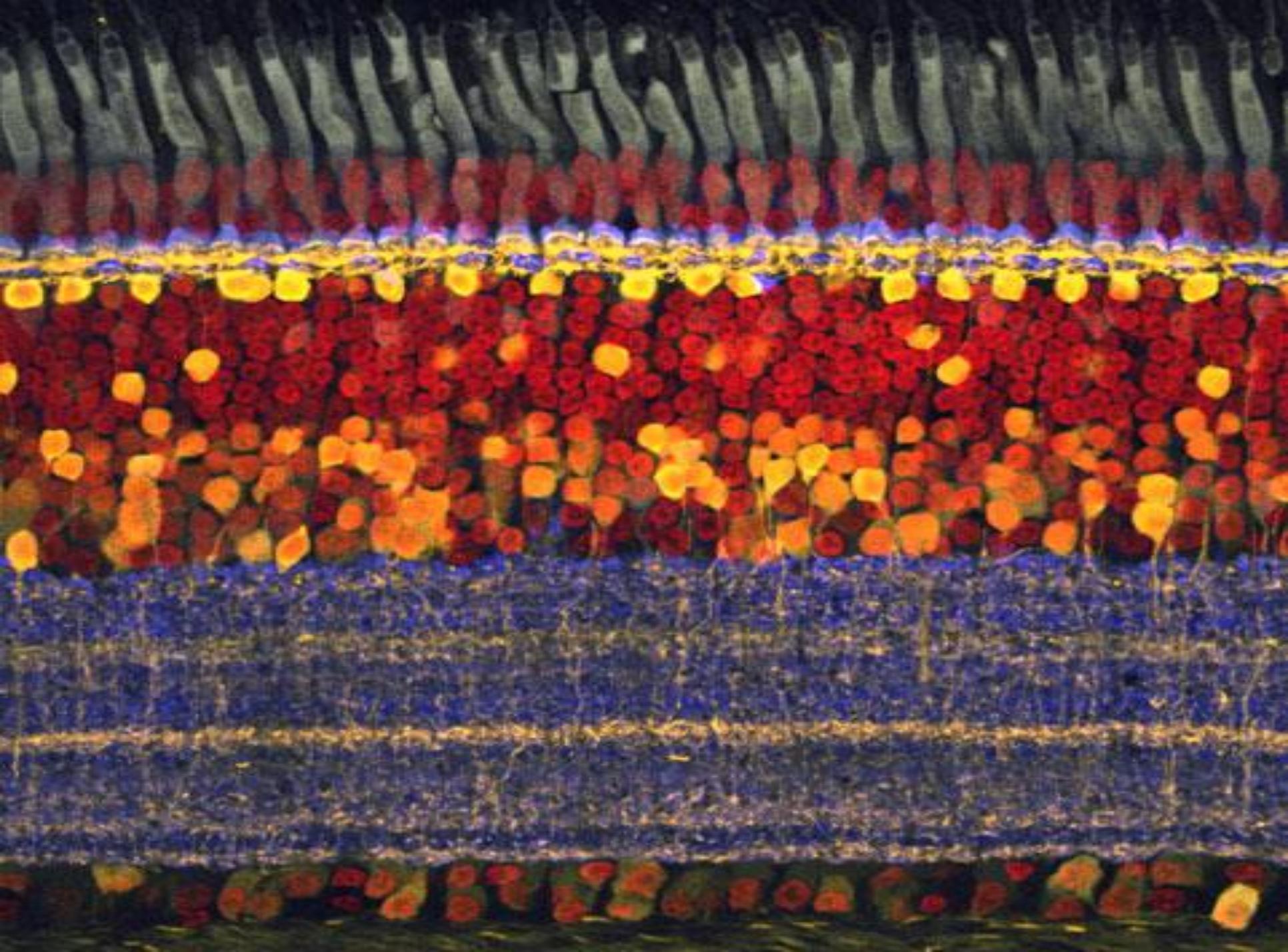
- Aggiornamento dati sanitari [storico]
- Infografica epidemiologica ISS
- Sorveglianza settimanale Regioni
- Aggiornamento nazionale ISS

Regioni - totale casi, attuali e incremento

Lombardia:	438.591	(87.449)	(2.938)
Piemonte:	183.084	(59.991)	(1.553)
Veneto:	181.454	(85.093)	(3.883)
Campania:	171.332	(64.480)	(1.340)
Emilia-Romagna:	141.010	(64.055)	(1.211)
Lazio:	137.143	(68.193)	(1.230)
Toscana:	111.097	(20.824)	(657)
Sicilia:	76.366	(36.410)	(999)
Puglia:	70.310	(26.003)	(1.813)

Note

11/12/2020
 La Regione Calabria comunica che il numero totale di tamponi del 10/12/2020 era 390.443. La Regione Emilia Romagna comunica che in seguito a verifica sui dati comunicati nei giorni passati è stato eliminato 1 caso in quanto giudicato non caso COVID-19. La Regione Campania comunica di non potere al momento riportare i dati quotidiani sugli ingressi in T.I.

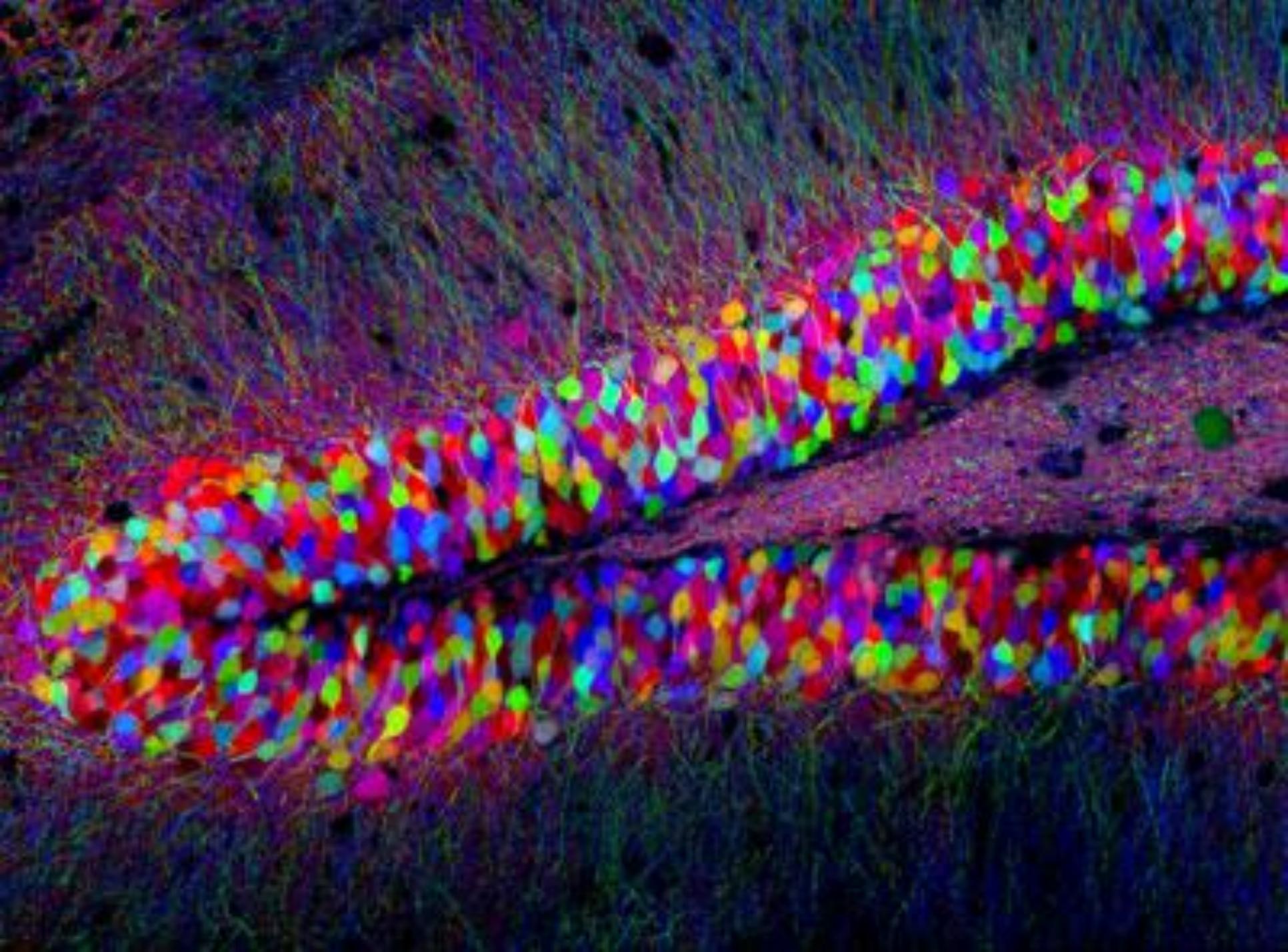


I POETI SONO LADRI DI FUOCO

Adriano Moretti

www.oliosapiente.it







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_favorisce la nascita e l'operatività di gruppi di studio e di ricerca;

_promuove e gestisce biblioteche;

_realizza attività editoriali sia cartacee sia audiovisive;

_svolge attività di solidarietà internazionale organizzando viaggi di studio, missioni all'estero, gemellaggi e partnership nella realizzazione di opere, impianti, strutture e attività finalizzate alla crescita e sostentamento dei paesi in via di sviluppo.

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Marco RUINI

