



Ispettorato Nazionale del Corpo Militare Volontario C.R.I.
Ausiliario delle Forze Armate

**XXIV CONVEGNO NAZIONALE
DEGLI UFFICIALI MEDICI E DEL PERSONALE SANITARIO DELLA
CROCE ROSSA ITALIANA**
Siracusa - Centro Congressi del Museo Archeologico "Paolo Orsi"
29 Settembre - 2 Ottobre 2022



La nebbia cerebrale

Enzo Sanzaro

Unità Operativa di Neurologia e Stroke Unit
Ospedale Umberto I di Siracusa

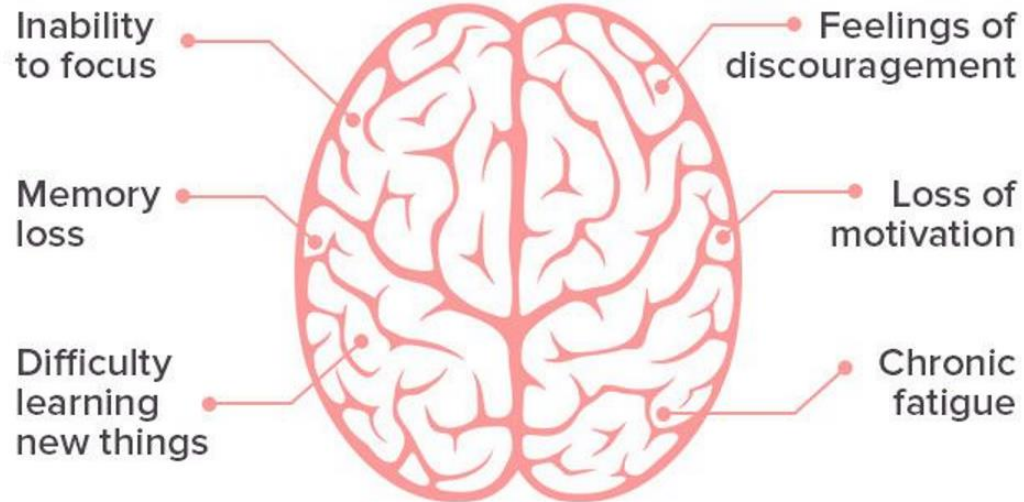


- attenzione
- fluidità del linguaggio
- velocità di elaborazione
- funzioni esecutive
- memoria



CAUSES & SYMPTOMS OF *Brain Fog*

SYMPTOMS





**Technology
overload**



**Blood sugar
imbalances**



**Gluten
intolerance**



Anemia



Inflammation



**Sleep
deprivation**



Overtraining



**Early
menopause**



**Side effects
from drugs**



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Short communication

How and why patients made Long Covid

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SARS-CoV-2

ABSTRACT

Patients collectively made Long Covid – and cognate term ‘Long-haul Covid’ – in the first months of the pandemic. Patients, many with initially ‘mild’ illness, used various kinds of evidence and advocacy to demonstrate a longer, more complex course of illness than laid out in initial reports from Wuhan. Long Covid has a strong claim to be the first illness created through patients finding one another on Twitter: it moved from patients, through various media, to formal clinical and policy channels in just a few months. This initial mapping of Long Covid – by two patients with this illness – focuses on actors in the UK and USA and demonstrates how patients marshalled epistemic authority. Patient knowledge needs to be incorporated into how COVID-19 is conceptualised, researched, and treated.

Long Covid has a strong claim to be considered the first illness to be collectively made by patients finding one another through **Twitter and other social media**.

BREATHE PROPERLY
Stop spreading negativity. There is no shortage of oxygen in the air

Strange!
Now the virus is affecting the brain and not lungs!



SPRIT

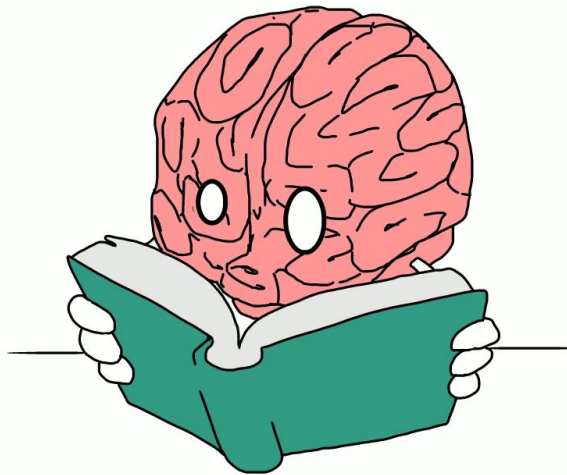
Cognitive dysfunction increased over the first three months post infection, then **decreased** slightly in the following 7 months.

While age is an important factor in cognitive and memory disfunction, it is worrying that non-hospitalized, young people (16–30 years old) suffer potentially severe symptoms, such as concentration and memory problems, half a year after infection.



(Blomberg, et al., 2021; Davis, et al., 2021)

The most prevalent dysfunction concerns memory, affecting up to 73% (in an interview study on 2739 patients), inducing both short-term and long-term memory loss (Davis, et al., 2021).



ACCADEMIA NAZIONALE DEI LINCEI

Long Covid (PASC)

Statement by the Lincei Committee on Covid-19

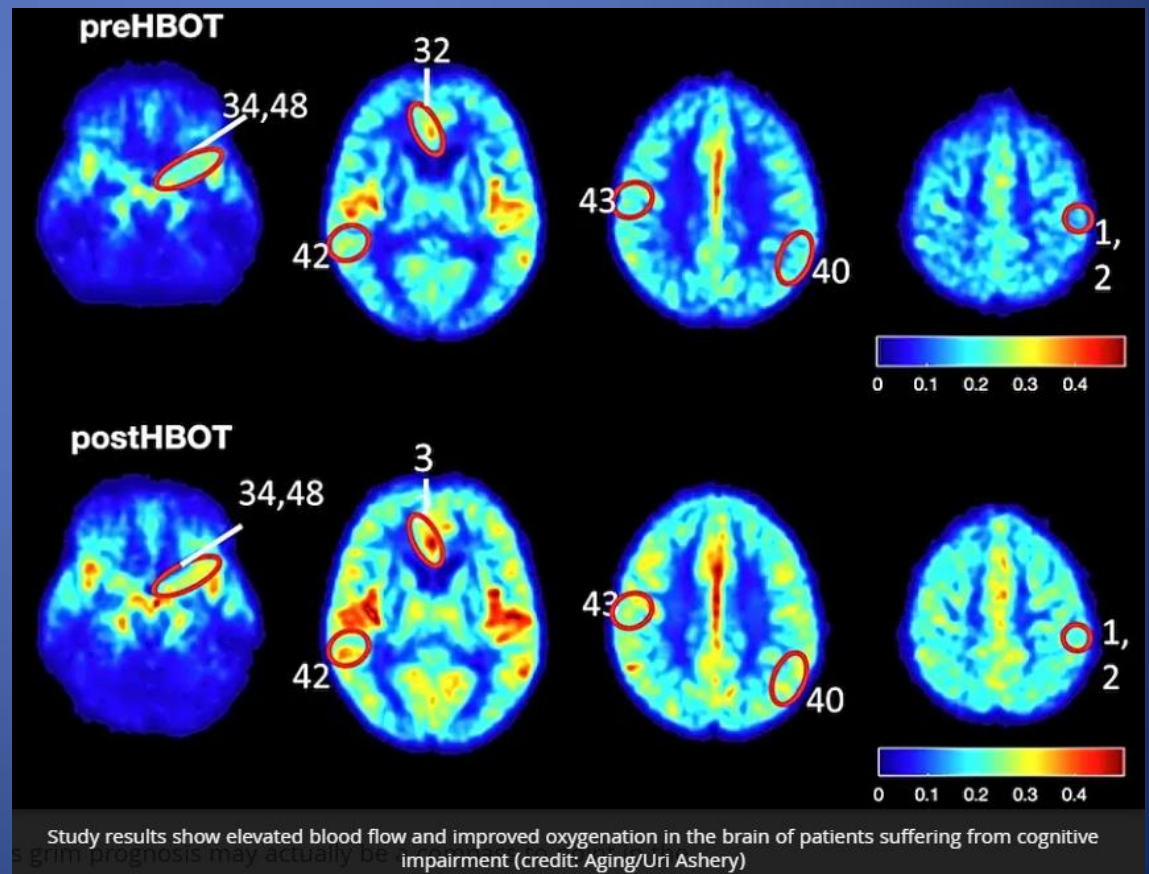
13 June 2022

The study of the anatomical or functional imaging of brain alterations shows consistent changes in many brain areas:

- Somatosensory cortex
- Rectal/orbital gyrus (including the olfactory system)
- Temporal lobe (including the amygdala, piriform cortex and the hippocampus)
- Hypothalamus/thalamus
- Brainstem
- Cerebellum

18F-FDG brain PET studies:

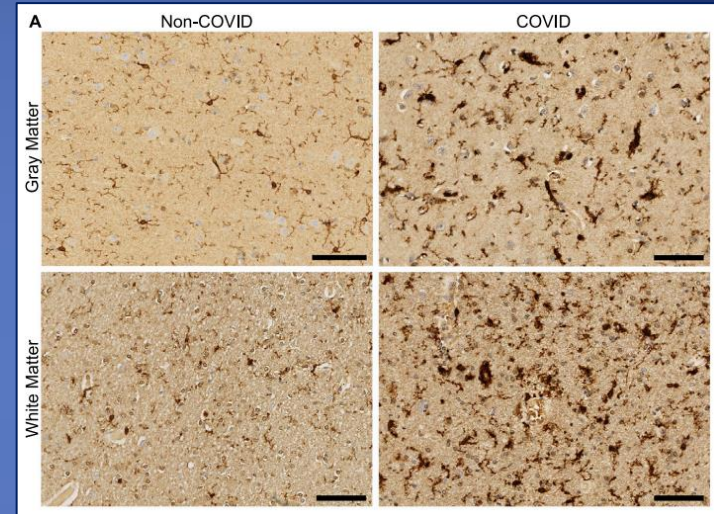
- prominent hypometabolism
- reversibility of the decreased neocortical glucose metabolism



Both grey and white matter of many brain areas change.

Grey matter is reduced in many regions of the:

- orbito/frontal cortex and limbic system that include olfactory cortex
- piriform cortex,
- amygdala,
- parahippocampal and hippocampal cortex
- insula.



White matter alterations in regions functionally connected with:

- the piriform cortex, olfactory tubercle and anterior olfactory nucleus.

These altered structures participate in the perception of taste, smell, emotion, memory and spatial navigation, functions that are strongly compromised during PASC.

The anatomical deficits increase with age between 60 and 75 and are likely to be modest in the age group of 55.

This reinforces neuropsychological data that showed COVID-19 as a risk factor to develop dementia, neurodegenerative diseases and mild cognitive impairments even in 50-year-old adults (Taquet, Geddes, Husain, Luciano, & Harrison, 2021).



Pathogenesis of long COVID

Candidate mechanisms of pathogenesis can be classified along four major lines:

- persistence of SARS-CoV-2;
- reactivation of other viruses, in particular Epstein-Barr virus (EBV);
- autoimmunity triggered by the virus;
- persistent tissue damage and immunity-triggered inflammation

Neurological and psychiatric risk trajectories after SARS-CoV-2 infection: an analysis of 2-year retrospective cohort studies including 1 284 437 patients



Maxime Taquet, Rebecca Sillett, Lena Zhu, Jacob Mendel, Isabella Camplisson, Quentin Dercon, Paul J Harrison



Summary

Background COVID-19 is associated with increased risks of neurological and psychiatric sequelae in the weeks and months thereafter. How long these risks remain, whether they affect children and adults similarly, and whether SARS-CoV-2 variants differ in their risk profiles remains unclear.

Lancet Psychiatry 2022

Published Online

August 17, 2022

<https://doi.org/10.1016/S2215->

Se e quando?

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Il profilo di rischio nei diversi strati di età, soprattutto nei bambini, non è stato ben caratterizzato

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Non è noto se i profili di rischio
siano cambiati o meno con
l'emergere di diverse varianti

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- **traiettorie di rischio a 2 anni**
- **14 diagnosi neurologiche e psichiatriche**
- **tre gruppi di età** (giovani di età inferiore a 18 anni, adulti di età compresa tra 18 e 64 anni e anziani di età ≥ 65 anni)

	Hazard ratio (95% CI)	p value	Risk horizon (days)	Time to equal incidence (days)
Anxiety disorder	1.13 (1.11–1.15)	<0.0001	58	417
Cognitive deficit	1.36 (1.33–1.39)	<0.0001	NR	NR
Dementia	1.33 (1.26–1.41)	<0.0001	NR	NR
Encephalitis	0.96 (0.85–1.08)	0.50
Epilepsy or seizures	1.14 (1.09–1.19)	<0.0001	NR	NR
Guillain-Barré syndrome	1.12 (0.97–1.30)	0.12
Insomnia	1.13 (1.10–1.16)	<0.0001	90	NR
Intracranial haemorrhage	1.09 (1.01–1.18)	0.020	506	658
Ischaemic stroke	1.11 (1.06–1.17)	<0.0001	66	712
Mood disorder	1.08 (1.06–1.11)	<0.0001	43	457
Myoneural junction or muscle disease	1.89 (1.76–2.04)	<0.0001	497	NR
Nerve, nerve root, and plexus disorder	0.89 (0.87–0.91)	<0.0001
Parkinsonism	1.04 (0.92–1.17)	0.58
Psychotic disorder	1.27 (1.18–1.37)	<0.0001	NR	NR
Any first outcome	1.13 (1.11–1.15)	<0.0001	48	469

The risk horizon is the time at which the time-varying hazard ratio returns to 1 (ie, the baseline risk in the comparison cohort). The time to equal incidence is the time at which the cumulative incidences of the two cohorts become equal. The risk horizon and time to equal incidence are only included for outcomes with a significantly increased hazard ratio at 6 months; for outcomes that did not reach the risk horizon or time to equal incidence within the follow-up period (up to 730 days), they are shown as not reached (NR).

Table 2: Risk of neurological and psychiatric sequelae at 6 months, risk horizon, and time to equal incidence for each diagnosis after COVID-19 versus after other respiratory infections, in the propensity-score matched population

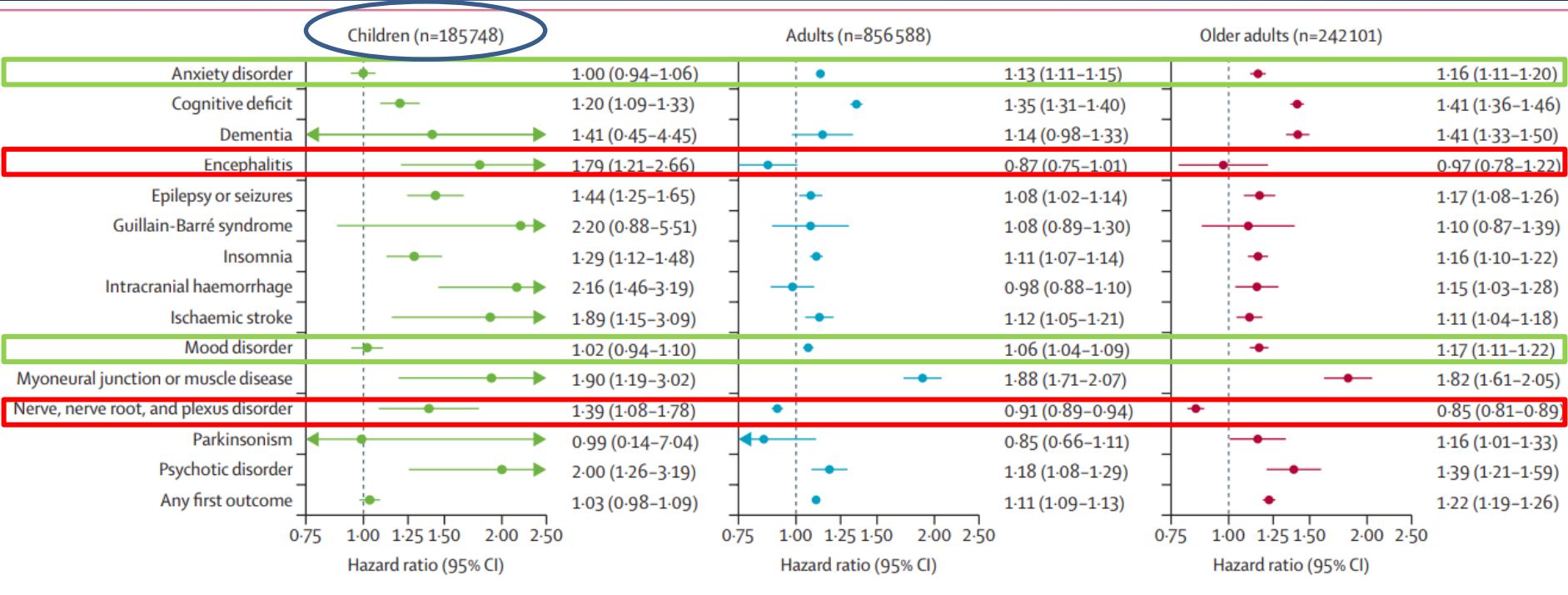
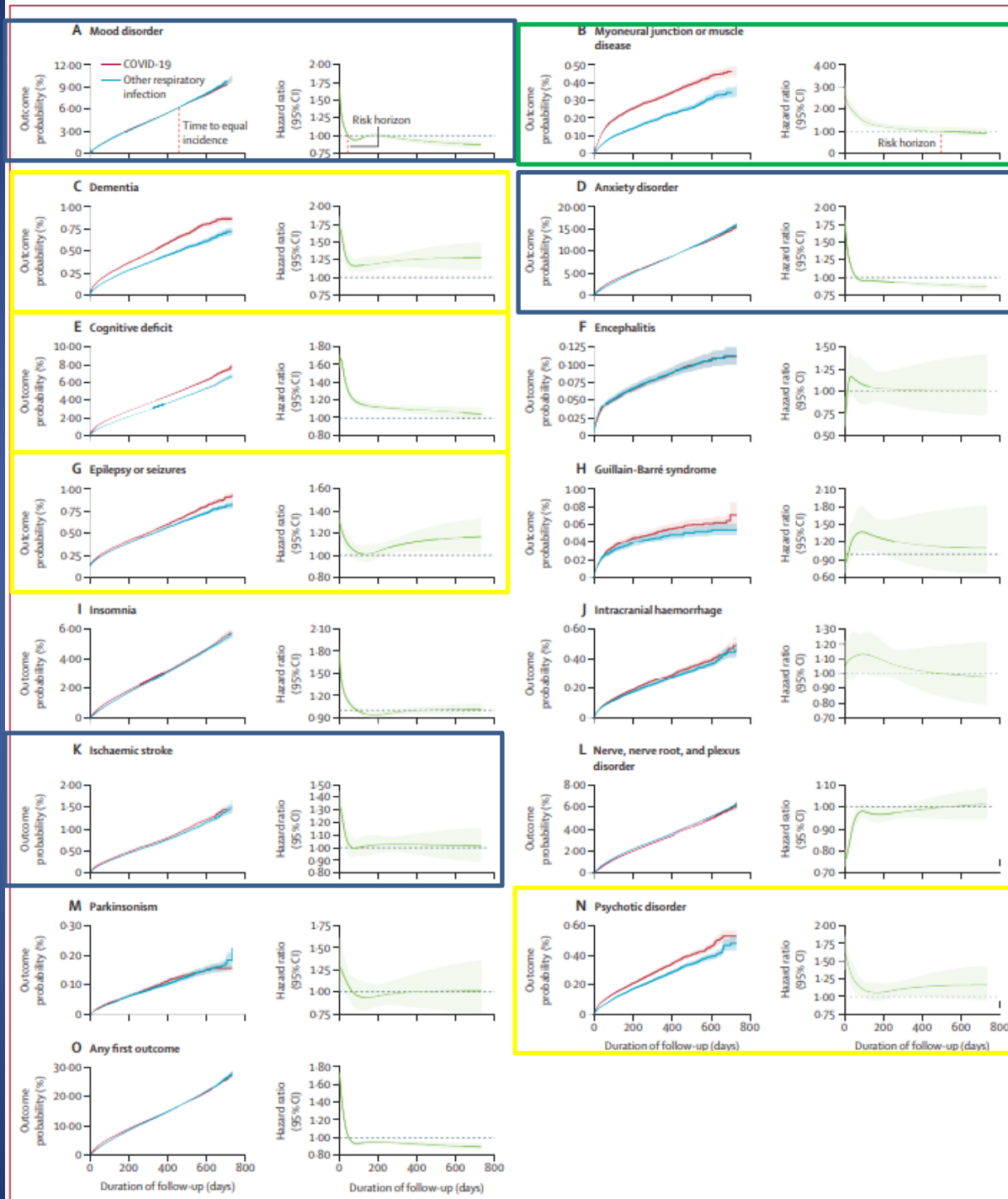
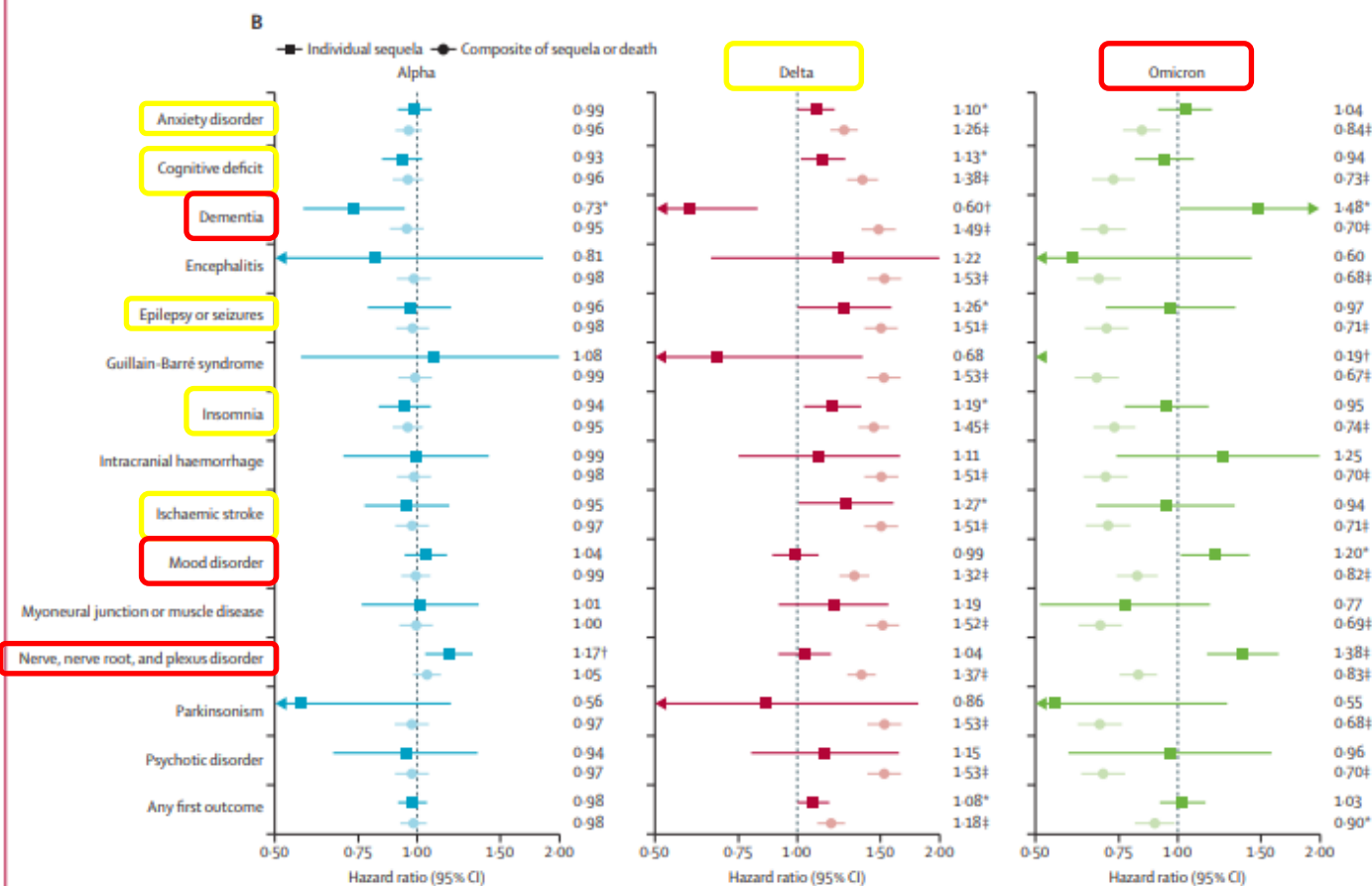
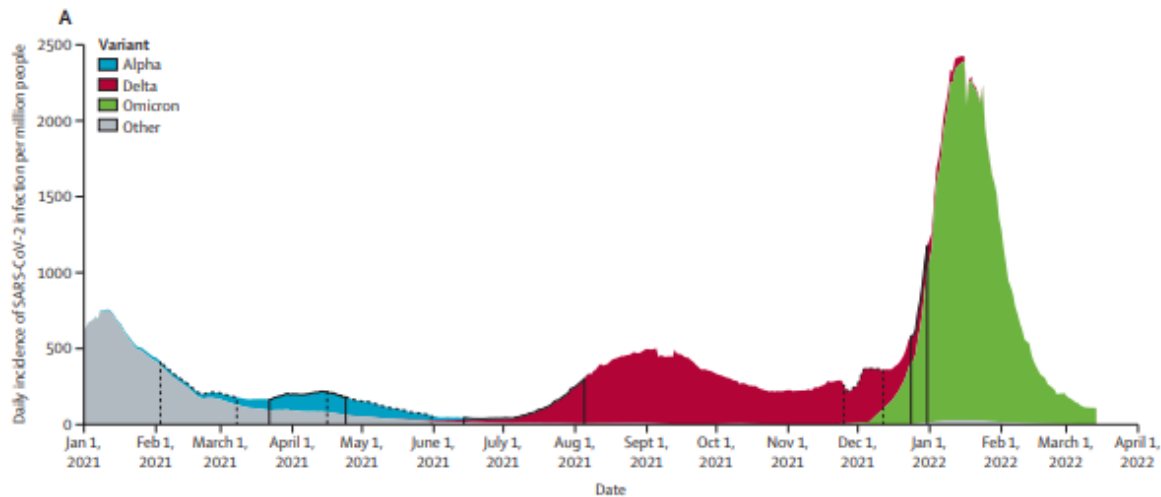


Figure 2: Hazard ratios for the 6-month risk of neurological and psychiatric sequelae after COVID-19 versus another respiratory infection, in different age groups, in the propensity-score matched population

Data are hazard ratios with 95% CIs. Children defined as younger than 18 years, adult, aged 18–64 years, and older adults as aged 65 years or older





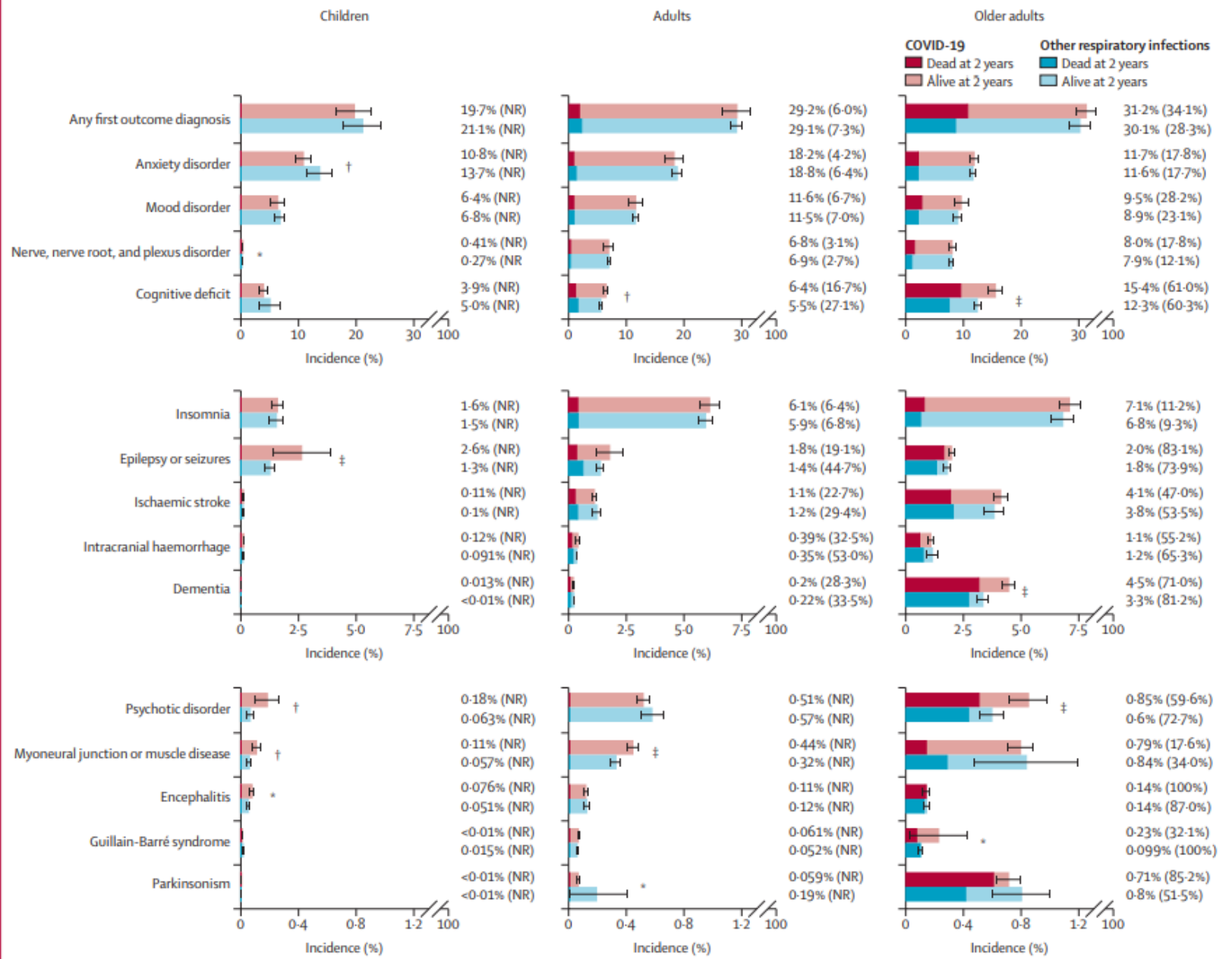


Figure 3: Cumulative incidence of neurological and psychiatric diagnoses at 2 years after COVID-19 versus another respiratory infection, in different age groups, by mortality status at 2 years (or censorship date), in the matched cohorts

The proportion next to each bar corresponds to the overall incidence of the outcome within that age group and the number in brackets indicates the proportion of those with the outcome who died within 2 years. Estimated numbers of deaths that are lower than 120 are unreliable and therefore not reported. 95% CIs for each estimate, and p values for each outcome, are in the appendix (p 32). NR=not reported *p<0.05. †p<0.01. ‡p<0.001.

NELLA NEBBIA

È strano vagare nella nebbia!
Solo è ogni cespuglio e pietra,
Nessun albero vede l'altro,
Ognuno è solo.

Pieno di amici era per me il mondo,
Quando la mia vita era ancora luminosa;
Adesso, che la nebbia cala,
Nessuno si vede più.








In verità, nessuno è saggio
Se non conosce il buio,
Che piano ed inesorabilmente
Da tutti lo separa.

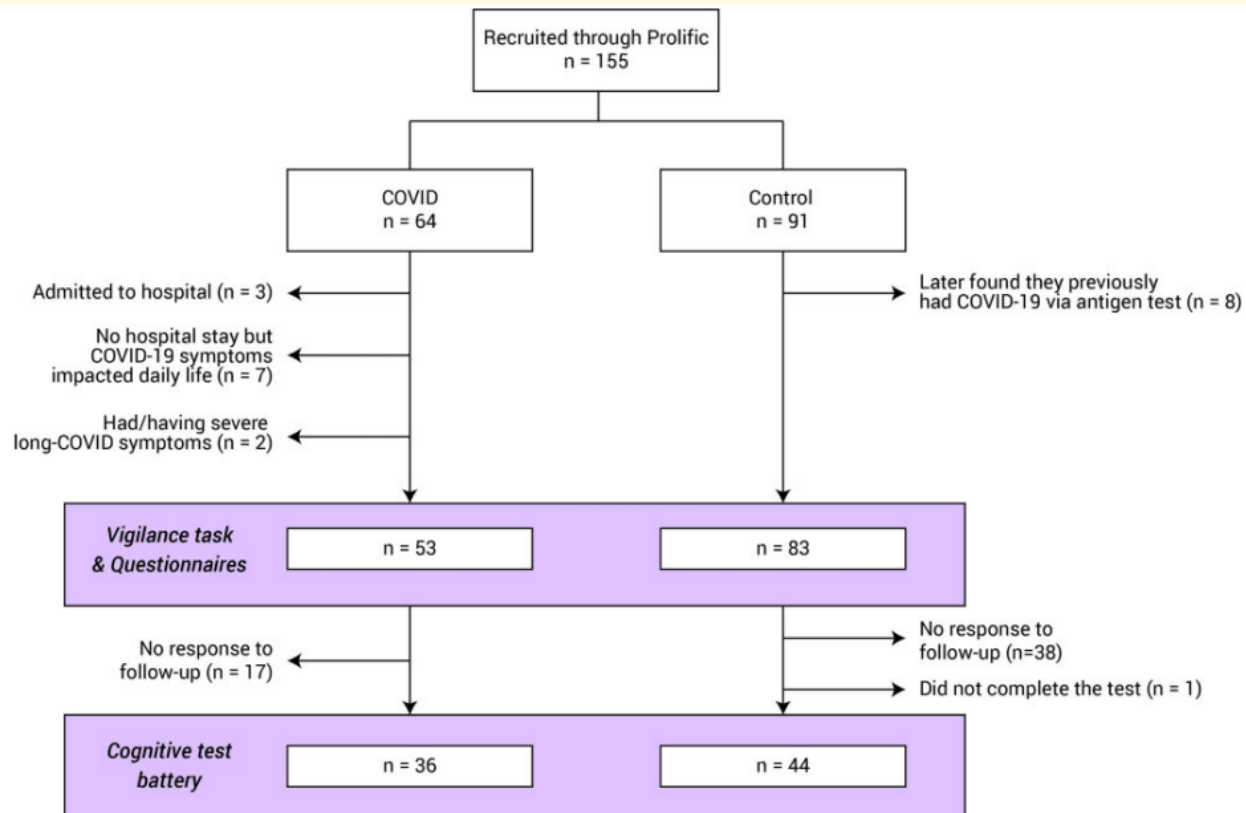
Strano, vagare nella nebbia!
Vivere è essere soli.
Nessuno uomo conosce l'altro,
Ognuno è solo.

Hermann Hesse

BRAIN COMMUNICATIONS








Rapid vigilance and episodic memory decrements in COVID-19 survivors

 Sijia Zhao,¹  Kengo Shibata,²  Peter J. Hellyer,^{3,4}  William Trender,³  Sanjay Manohar,^{1,2}
 Adam Hampshire³ and  Masud Husain^{1,2}



BRAIN COMMUNICATIONS

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Non mostravano differenze da un gruppo di controllo per quanto riguarda stanchezza, dimenticanza, anomalie del sonno, motivazione, depressione, ansia o profilo di personalità

BRAIN COMMUNICATIONS

Rapid vigilance and episodic memory decrements in COVID-19 survivors

©Sijia Zhao,¹ Kengo Shibata,² Peter J. Hellyer,^{3,4} ©William Trender,³ ©Sanjay Manohar,^{1,2} ©Adam Hampshire³ and ©Masud Husain^{1,2}



Questionnaires

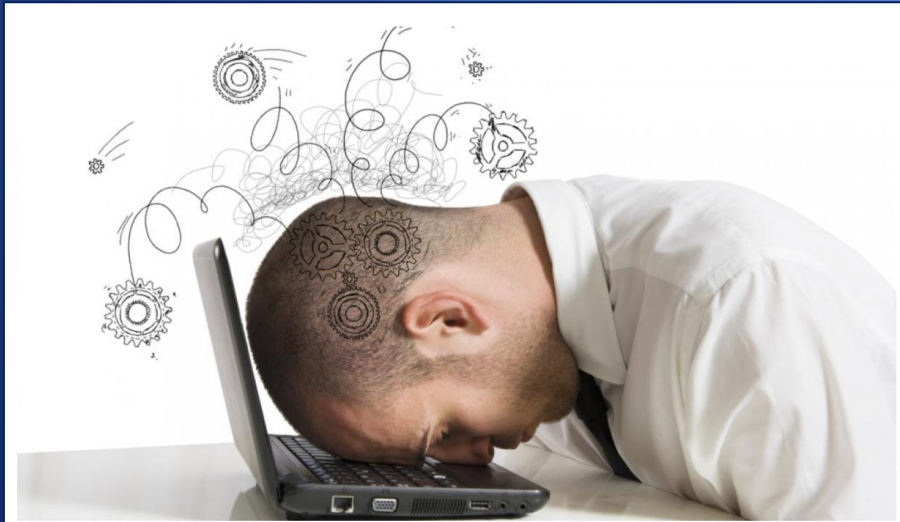
The questionnaires included were:

- *Fatigue and sleep*: Neurological Fatigue Index (NFI), which has been used to assess fatigue in persons with multiple sclerosis.¹⁸ Our motivation for including this index was driven by the fact that it probes the interactions between sleep and fatigue. Specifically, it asks questions related to abnormal nocturnal sleep, sleepiness and the need for diurnal sleep/rest.
- *Distractibility and forgetfulness*: Cognitive Failures Questionnaire (CFQ),¹⁹ a 25-item questionnaire about minor mistakes in daily life over the last 2 weeks. For example: ‘Do you find you forget appointments?’ ‘Do you fail to notice signposts on the road?’ ‘Do you find you forget which way to turn on a road you know well but rarely use?’.
- *Personality*: A Short 15-item Big Five Inventory (BFI-S)²⁰ and the Short Grit Scale (GRIT-S).²¹ One of BFI-S components—conscientiousness—provides information about the conscientiousness personality trait, describing an individual’s perseverance of effort combined with passions for a particular goal. To ensure that this is well-captured, we also included GRIT-S: this estimates the same trait but with different questions. We indeed found that these two scales were strongly positively correlated (Spearman’s $\rho = 0.65$, $P < 0.0001$).
- *Motivation*: Apathy Motivation Index (AMI), an 18-item questionnaire, sub-divided into three subscales of apathy: emotional, behavioural and social apathy.²²
- *Mood*: Hospital Anxiety and Depression Scale (HADS), a 14-item questionnaire, sub-divided into depression and anxiety.²³

BRAIN COMMUNICATIONS

Rapid vigilance and episodic memory decrements in COVID-19 survivors

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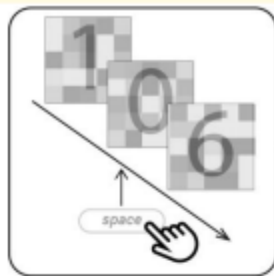


Vigilance test

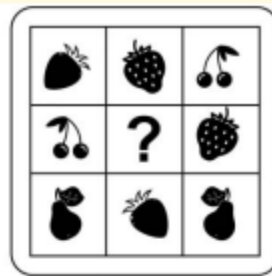
All participants were first tested on a version of an established, sustained visual attention task²⁴ adapted into a modern online version hosted on the Pavlovia platform (pavlovia.org). An online demo is available at https://run.pavlovia.org/sijiazhao/vigilance_english_demo (open it with the Chrome Internet browser on a desktop computer). This task is designed to assess the performance decrement during sustained visual attention. A single digit (0–9) was presented at the centre of the screen for 50 ms every second

Motivation and fatigue ratings with time on the task

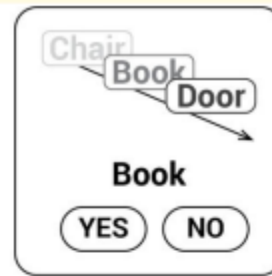
After each minute during testing, participants were asked to report their level of fatigue ('How tired do you feel now?') and motivation ('How motivated do you feel?') using a visual analogue scale. Responses were registered by clicking on the appropriate position on each scale. After completing all ratings, a 'confirm' button appeared at the bottom of the screen, allowing participants to validate their ratings and start the next block. To control the time between blocks and to reduce variance between participants, a 15 s countdown timer was displayed at the top of the screen, and the next block would begin automatically once the timer lapsed. There were seven participants who had missing ratings. The exclusion of these participants did not affect the rating results or behavioural data and there were no group differences in age, gender or any questionnaire measures ($P > 0.05$).



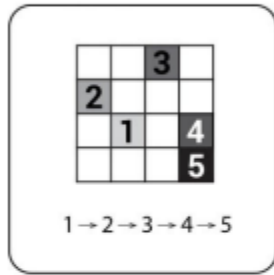
Vigilance



Object Memory



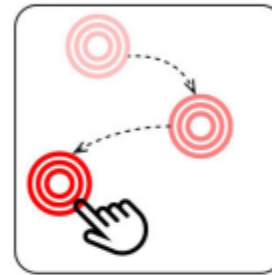
Word Memory



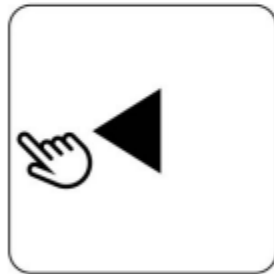
Spatial Span



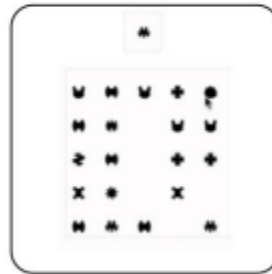
Simple Reaction



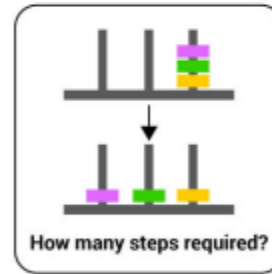
Motor Control



Choice Reaction



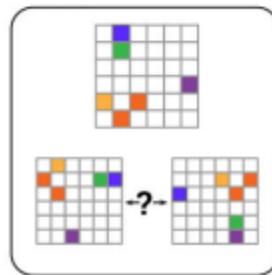
Target Detection



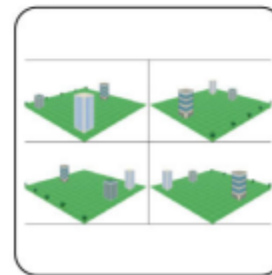
Tower of London



Verbal analogies



2D Mental Rotations



3D Mental Rotations

Table 1 Self-reported participant demographics and questionnaire-derived measures

Measure	All (n = 136)	COVID (n = 53)	Control (n = 83)	Statistic
Age, mean years (SD)	28.6 (9.7)	28.0 (8.6)	29.0 (10.3)	$t(134) = -0.6, P = 0.5, BF = 4.4$
Gender, female (%)	54 (39.7)	23 (43.4)	31 (37.3)	$\chi^2(1, N = 54) = 0.5, P = 0.5$
COVID-19		163.0 (128.1)		
Time from COVID-19 diagnosis, mean days (SD)				
COVID-19 test type:		40/4/2/7		
PCR/lateral flow/unknown/not tested				
Stayed at hospital overnight for COVID-19 treatment, yes (%)		0 (0.0)		
Stayed at ICU for COVID-19 treatment, yes (%)		0 (0.0)		
Questionnaires				
NFI Physical fatigue (SD)	8.9 (4.7)	8.4 (4.4)	9.2 (4.9)	$t(134) = -1.0, P = 0.3, BF = 3.4$
Cognitive fatigue (SD)	4.2 (2.8)	4.0 (2.8)	4.4 (2.8)	$t(134) = -0.7, P = 0.5, BF = 4.1$
Sleep relief (SD)	7.8 (3.4)	7.7 (3.3)	7.8 (3.5)	$t(134) = -0.1, P = 0.9, BF = 5.3$
Sleep abnormality (SD)	6.9 (2.8)	7.2 (2.9)	6.7 (2.7)	$t(134) = 0.9, P = 0.4, BF = 3.8$
CFQ Forgetfulness (SD)	12.7 (5.0)	13.0 (4.8)	12.4 (5.2)	$t(86) = 0.6, P = 0.5, BF = 4.4$
False triggering (SD)	8.8 (4.7)	9.3 (4.7)	8.3 (4.7)	$t(86) = 1.0, P = 0.3, BF = 3.3$
Distractibility (SD)	12.3 (4.5)	12.4 (4.2)	12.2 (4.9)	$t(86) = 0.1, P = 0.9, BF = 5.3$
BFI-S Conscientiousness (SD)	10.5 (2.5)	10.4 (2.3)	10.7 (2.7)	$t(77) = -0.6, P = 0.6, BF = 4.6$
GRIT-S Grit scale (SD)	3.2 (0.7)	3.1 (0.6)	3.3 (0.8)	$t(77) = -0.9, P = 0.4, BF = 3.7$
AMI Behavioural apathy (SD)	10.3 (4.4)	10.9 (4.5)	9.8 (4.2)	$t(77) = 1.1, P = 0.3, BF = 3.0$
Social apathy (SD)	12.9 (5.0)	12.5 (5.4)	13.4 (4.4)	$t(77) = -0.8, P = 0.4, BF = 4.1$
Emotional apathy (SD)	8.0 (4.2)	8.6 (4.4)	7.3 (3.9)	$t(77) = 1.4, P = 0.2, BF = 2.2$
HADS Depression (SD)	5.4 (3.6)	5.4 (3.9)	5.4 (3.3)	$t(77) = 0.0, P = 1.0, BF = 5.3$
Anxiety (SD)	8.2 (3.8)	8.0 (4.0)	8.3 (3.7)	$t(77) = -0.4, P = 0.7, BF = 4.9$

T- and χ^2 -tests were used to assess between-group differences, with Bayes Factor (BF) reported. The questionnaires included are Neurological Fatigue Index (NFI), Cognitive Failures Questionnaire (CFQ), Short Big Five Inventory (BFI-S), Short Grit Scale (GRIT-S), AMI and the Hospital Anxiety and Depression Scale (HADS). For all the questionnaire-derived indices, the mean score is shown with 1SD in the bracket.



Vigilance

Object Memory

Word Memory

Spatial Span

Simple Reaction

Motor Control

Choice Reaction

Target Detection

Tower of London

lion is to feline
as
cabbage is to vegetable

true false

Verbal analogies

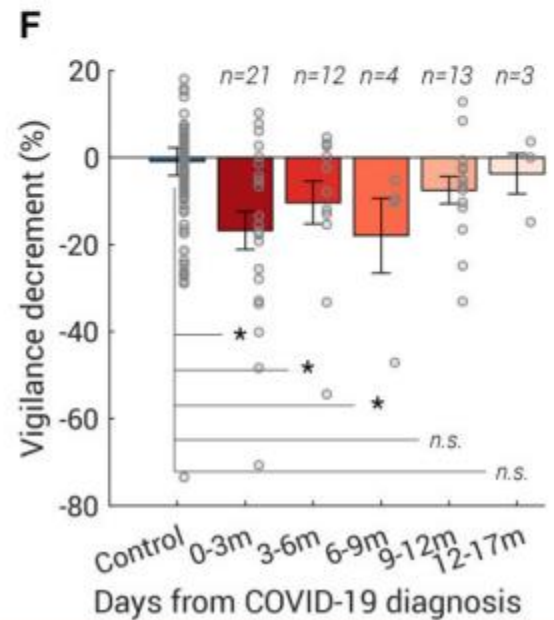
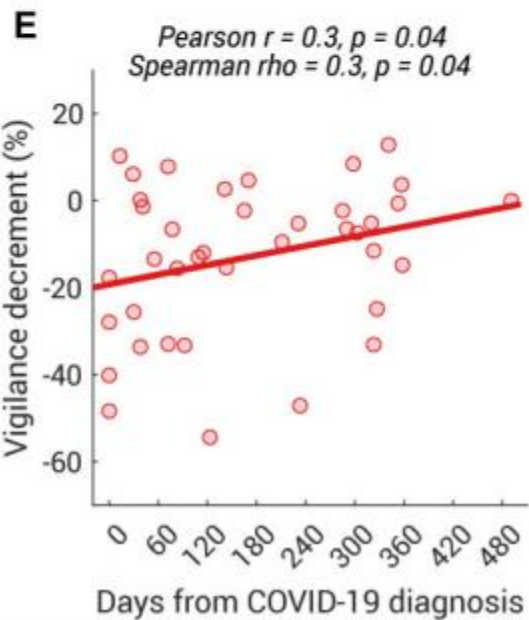
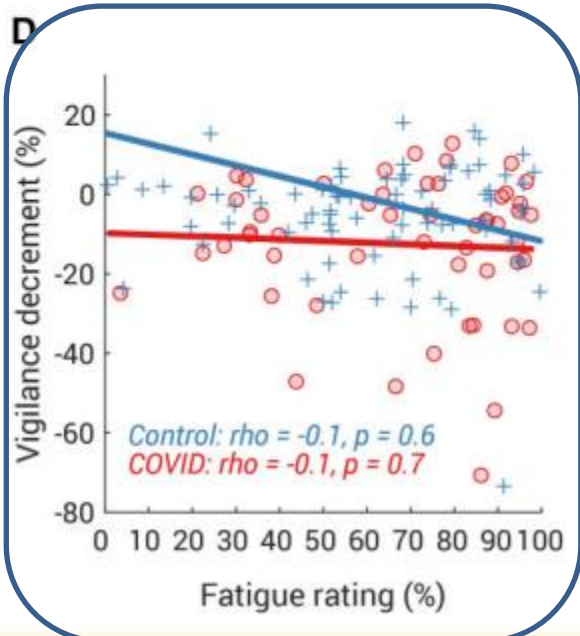
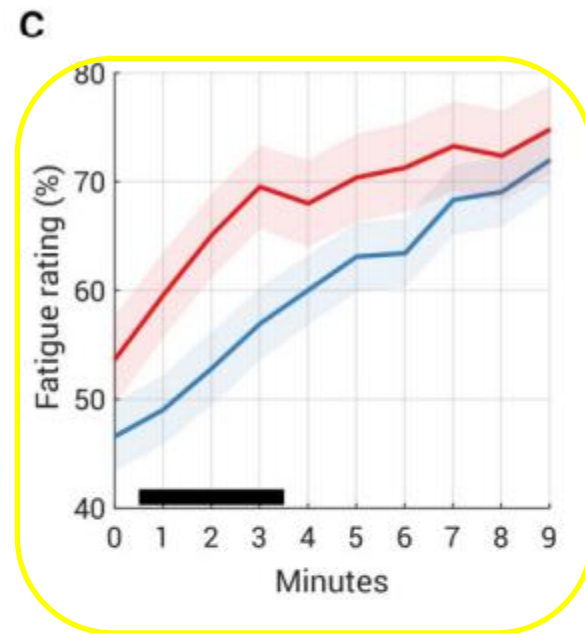
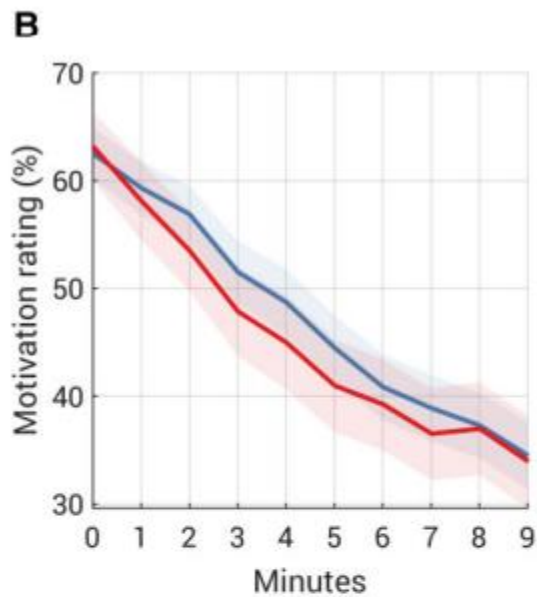
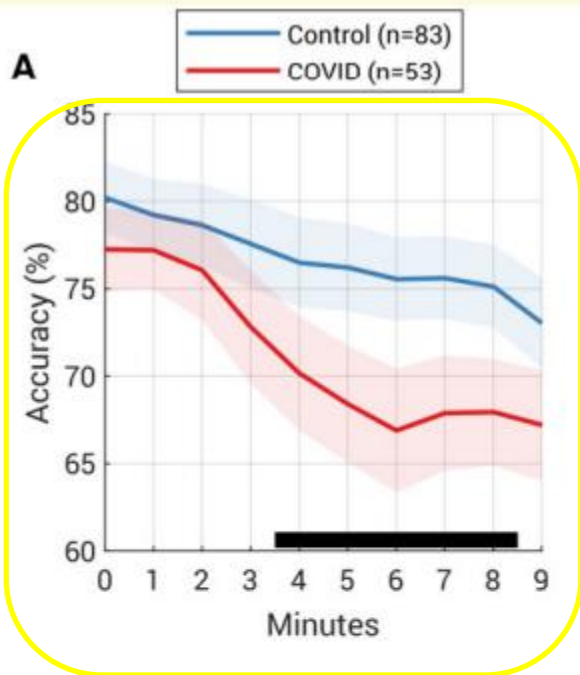
2D Mental Rotations

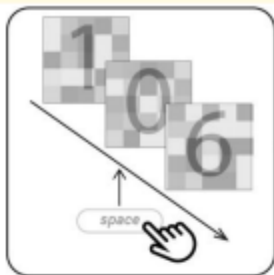
3D Mental Rotations

Table 2 Results of vigilance test

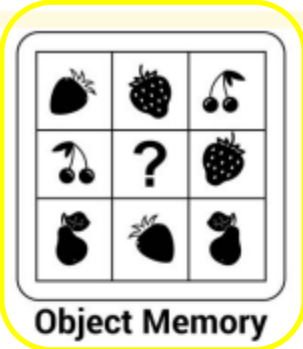
Measures	All (n = 136)	COVID (n = 53)	Control (n = 83)	Statistic
Accuracy				
Baseline accuracy (averaged over the first 3 min), % (SD)	77.3 (19.8)	75.5 (19.2)	78.5 (20.2)	$t(135) = -0.9, P = 0.4, BF = 3.8$
Final accuracy (averaged over the first 3 min), % (SD)	72.4 (22.0)	67.8 (23.0)	75.4 (20.9)	$t(135) = -2.0, P = 0.05, BF = 1.1$
Accuracy over 9 min, % (SD)	74.7 (20.0)	71.4 (19.8)	76.8 (20.0)	$t(135) = -1.5, P = 0.1, BF = 1.9$
Absolute change in accuracy (final minus baseline), % (SD)	-4.9 (10.1)	-7.7 (10.3)	-3.0 (9.5)	$t(135) = -2.7, P = 0.008, BF = 5.0$
Vigilance decrement, i.e. change in accuracy normalized by individual baseline, mean % (SD)	-5.4 (25.7)	-12.3 (17.4)	-0.9 (29.1)	$t(135) = -2.6, P = 0.01, BF = 3.8$
RT				
RT over 9 min, s (SD)	0.5 (0.1)	0.5 (0.1)	0.5 (0.1)	$t(134) = -0.2, P = 0.8, BF = 5.2$
Absolute change in RT (final minus baseline), s (SD)	0.02 (0.1)	0.01 (0.1)	0.02 (0.1)	$t(130) = -0.8, P = 0.4, BF = 4.0$
Change in RT normalized by individual baseline, % (SD)	4.0 (10.3)	3.0 (12.2)	4.6 (8.9)	$t(130) = -0.9, P = 0.4, BF = 3.8$
Ratings				
Baseline fatigue rating (average over the first 3 min), % (SD)	57.7 (28.6)	65.1 (27.2)	52.8 (28.6)	$t(135) = 2.5, P = 0.01, BF = 3.1$
Fatigue rating, average over 9 min % (SD)	63.3 (26.2)	68.2 (25.7)	60.1 (26.1)	$t(135) = 1.8, P = 0.08, BF = 1.3$
Change in fatigue rating (last 3 min minus first 3 min), % (SD)	11.6 (17.5)	7.9 (17.4)	14.1 (17.2)	$t(135) = -2.1, P = 0.04, BF = 1.3$
Baseline motivation rating, % (SD)	54.6 (24.6)	52.9 (26.4)	55.7 (23.4)	$t(135) = -0.7, P = 0.5, BF = 4.4$
Motivation rating, average over all ratings % (SD)	46.3 (24.5)	45.2 (26.4)	47.0 (23.3)	$t(135) = -0.4, P = 0.7, BF = 4.9$
Change in motivation rating (last 3 min minus first 3 min), % (SD)	-16.3 (17.8)	-15.7 (17.0)	-16.7 (18.4)	$t(135) = 0.3, P = 0.8, BF = 5.1$

T-tests used to assess between-group differences, with Bayes Factor (BF) reported. The significant t-tests are highlighted in bold.

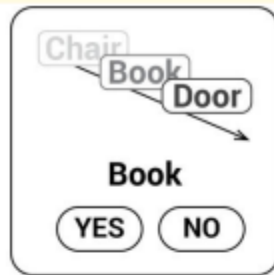




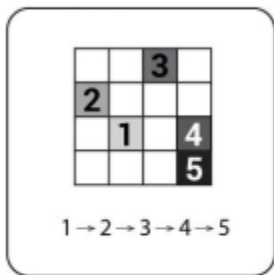
Vigilance



Object Memory



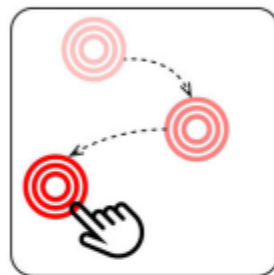
Word Memory



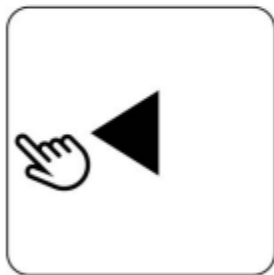
Spatial Span



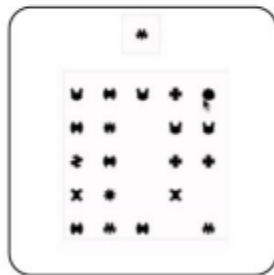
Simple Reaction



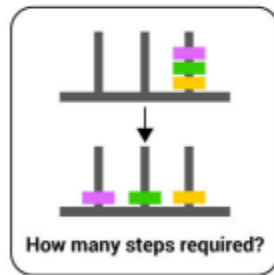
Motor Control



Choice Reaction



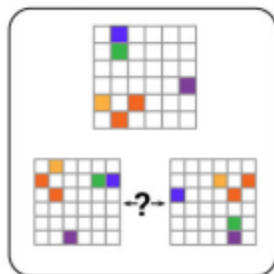
Target Detection



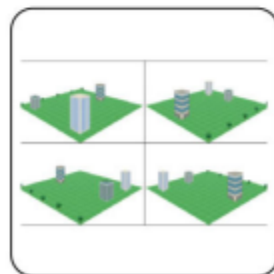
Tower of London



Verbal analogies



2D Mental Rotations



3D Mental Rotations

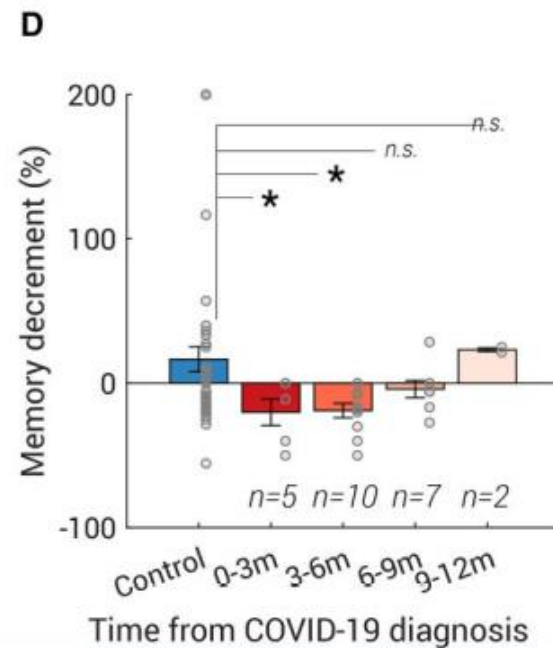
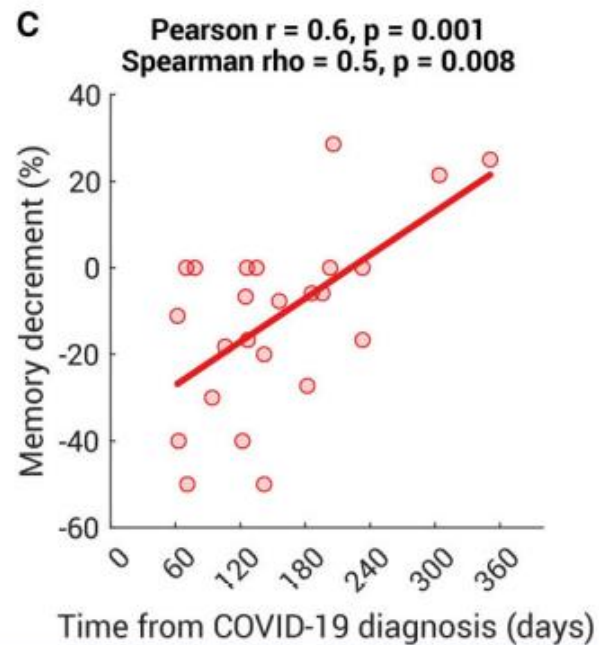
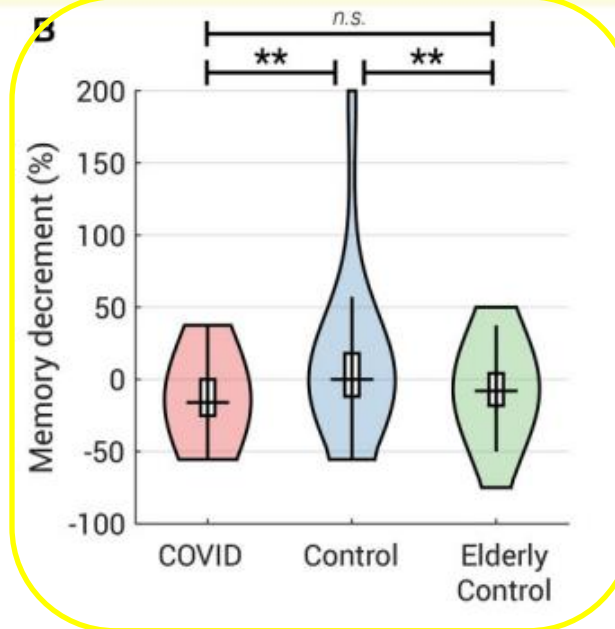
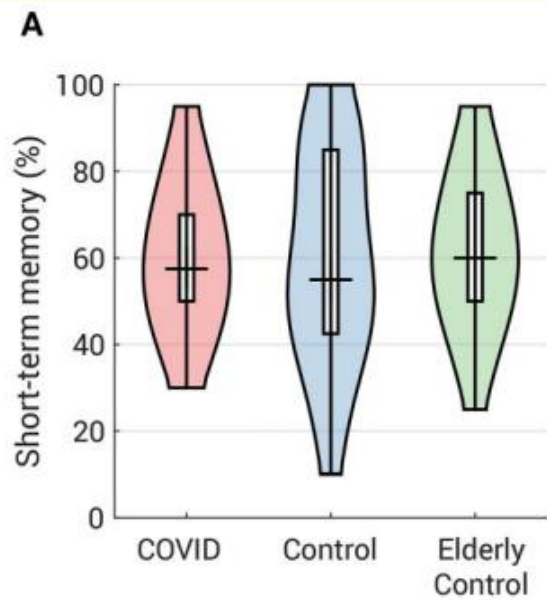


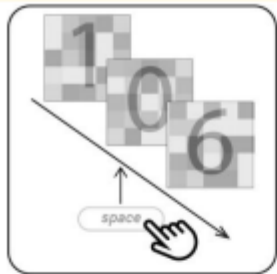
Memoria immediata

Risultati simili nel gruppo di controllo e nel post-Covid

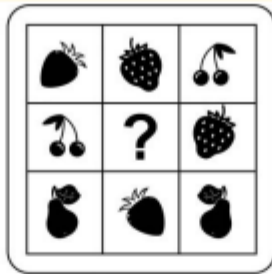
Dopo 30 minuti

Decremento della memoria maggiore rispetto ai *controlli*
del 9,2%

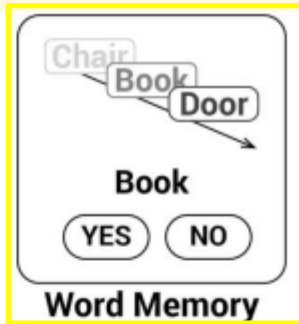




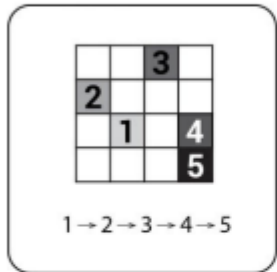
Vigilance



Object Memory



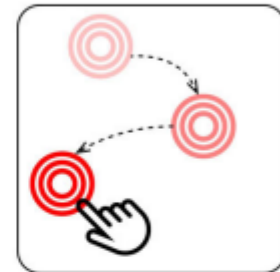
Word Memory



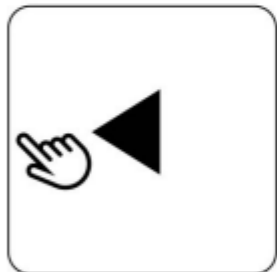
Spatial Span



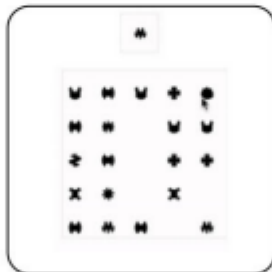
Simple Reaction



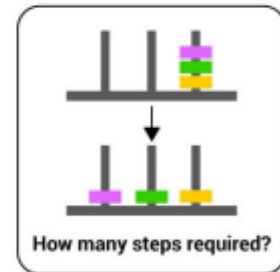
Motor Control



Choice Reaction



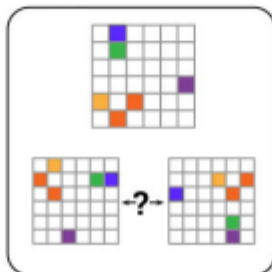
Target Detection



Tower of London



Verbal analogies



2D Mental Rotations



3D Mental Rotations

24 semplici parole

Vigilance

Object Memory

Word Memory

Spatial Span

Simple Reaction

Motor Control

Choice Reaction

Target Detection

Tower of London

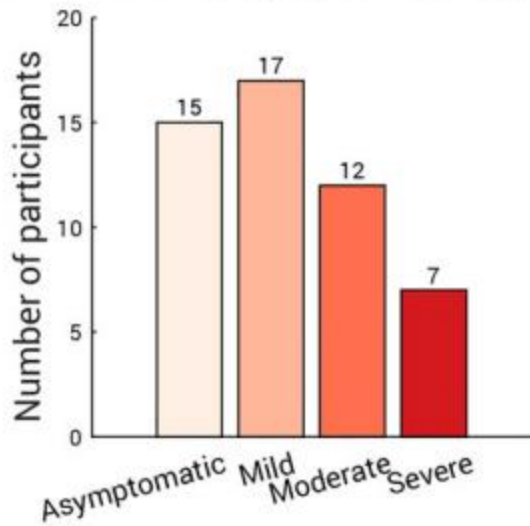
Verbal analogies

2D Mental Rotations

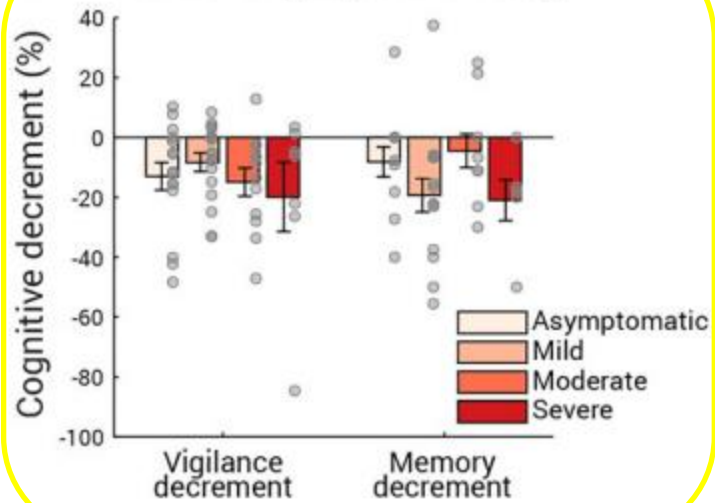
3D Mental Rotations

I gruppi non differivano significativamente tra loro

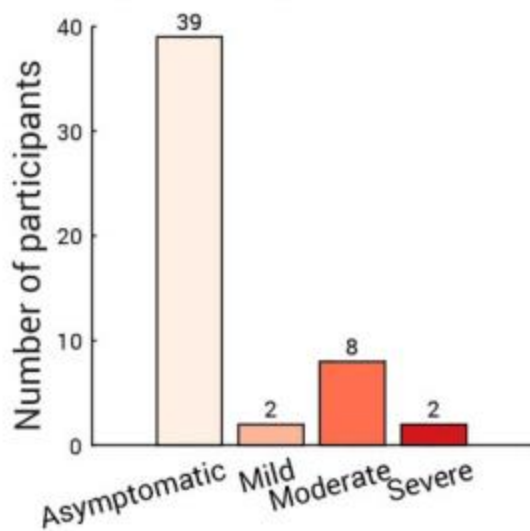
A COVID-19 symptom severity



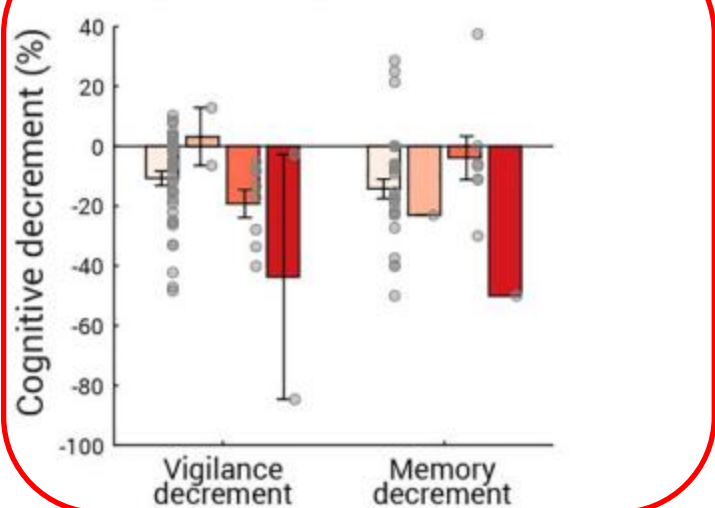
B COVID-19 symptom severity



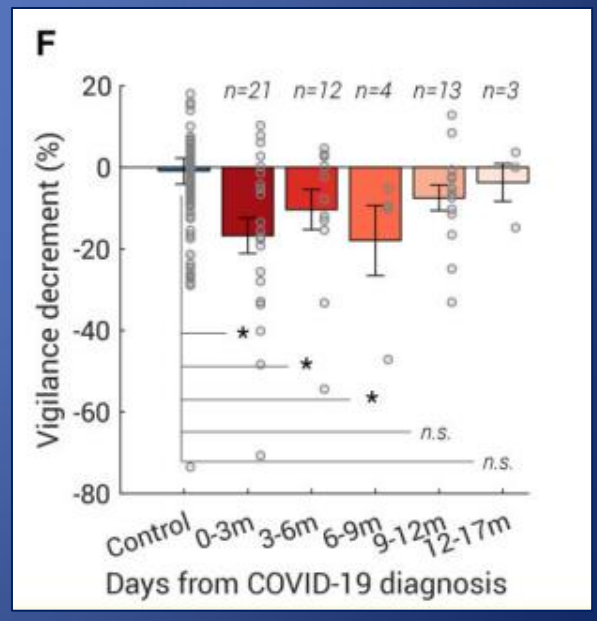
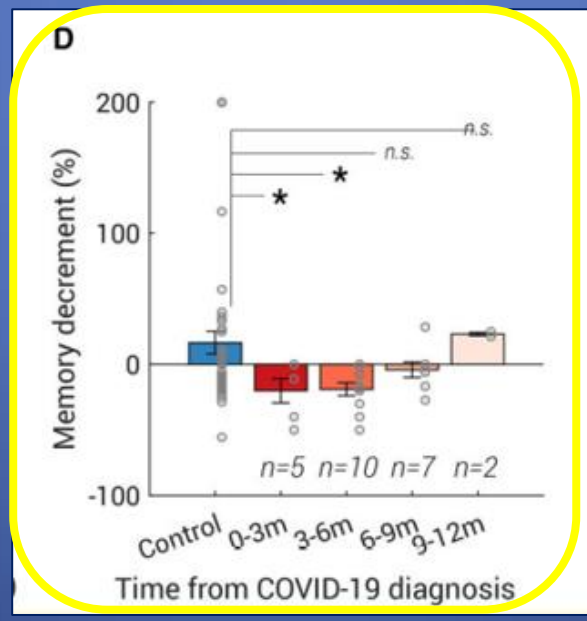
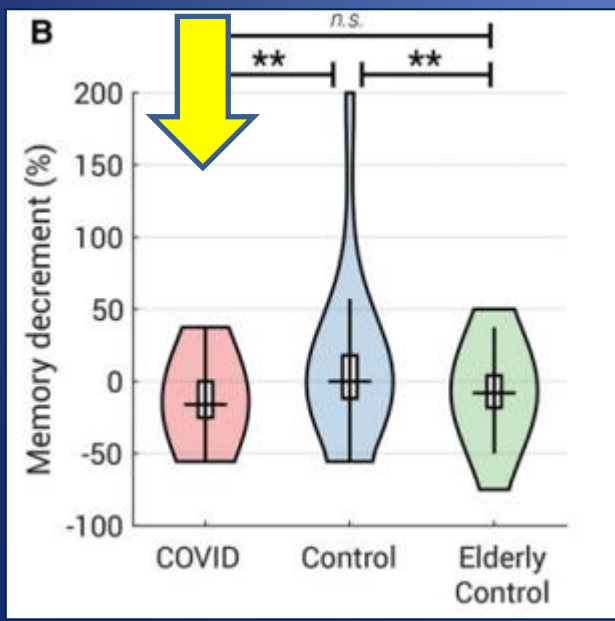
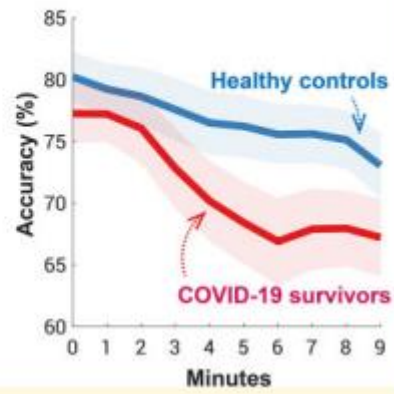
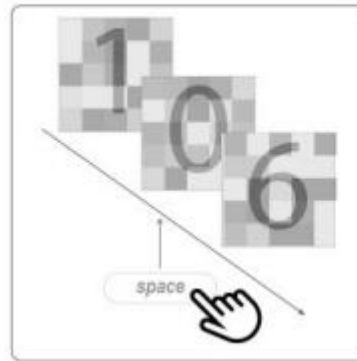
C Long-COVID symptom severity



D Long-COVID symptom severity



Attention declines rapidly over minutes in people who had COVID-19



Article

Mild respiratory COVID can cause multi-lineage neural cell and myelin dysregulation

Anthony Fernández-Castañeda,^{1,17} Peiwen Lu,^{2,17} Anna C. Geraghty,^{1,17} Eric Song,^{2,17} Myoung-Hwa Lee,³ Jamie Wood,⁴ Michael R. O’Dea,⁵ Selena Dutton,¹ Kiarash Shamardani,¹ Kamsi Nwangwu,¹ Rebecca Mancusi,¹ Belgin Yalçın,¹ Kathryn R. Taylor,¹ Lehi Acosta-Alvarez,¹ Karen Malacon,¹ Michael B. Keough,¹ Lijun Ni,¹ Pamelyn J. Woo,¹ Daniel Contreras-Esquivel,¹ Angus Martin Shaw Toland,⁶ Jeff R. Gehlhausen,² Jon Klein,² Takehiro Takahashi,² Julio Silva,² Benjamin Israelow,² Carolina Lucas,² Tianyang Mao,² Mario A. Peña-Hernández,² Alexandra Tabachnikova,² Robert J. Homer,⁷ Laura Tabacof,⁴ Jenna Tosto-Mancuso,⁴ Erica Breyman,⁴ Amy Kontorovich,⁸ Dayna McCarthy,⁴ Martha Quezado,⁹ Hannes Vogel,⁶ Marco M. Hefti,¹⁰ Daniel P. Perl,¹¹ Shane Liddelow,^{5,12,13} Rebecca Folkerth,¹⁴ David Putrino,⁴ Avindra Nath,³ Akiko Iwasaki,^{2,15,18,*} and Michelle Monje^{1,6,16,18,19,*}

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¹⁴Office of Chief Medical Examiner, New York, NY, USA

¹⁵Howard Hughes Medical Institute, Yale University, New Haven, CT, USA

¹⁶Howard Hughes Medical Institute, Stanford University, Stanford, CA, USA

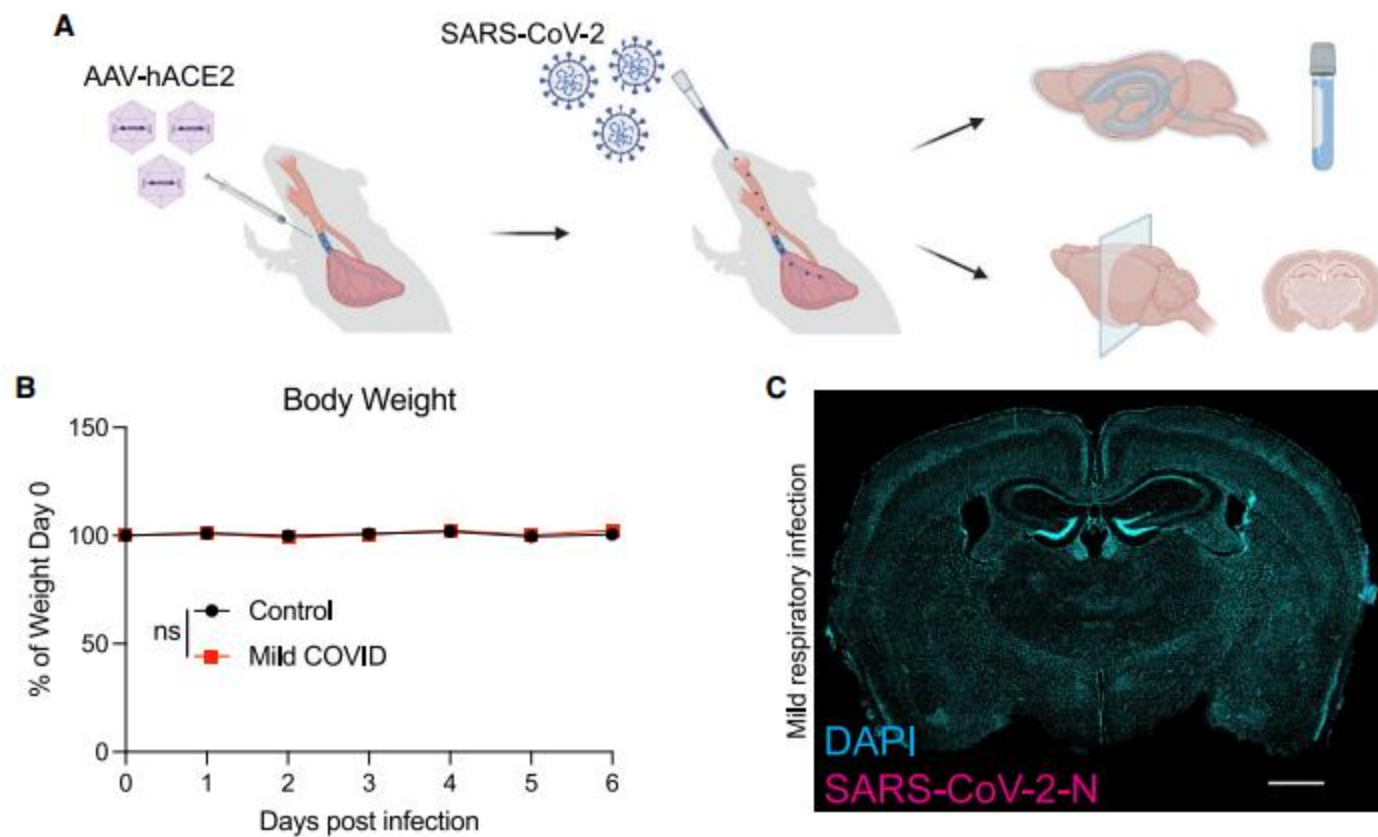
¹⁷These authors contributed equally

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<https://doi.org/10.1016/j.cell.2022.06.008>



REVIEW | VOLUME 44, ISSUE 6, P441-451, JUNE 01, 2021

Microglia in Cancer Therapy-Related Cognitive Impairment

Erin M. Gibson   • Michelle Monje  

Published: March 02, 2021 • DOI: <https://doi.org/10.1016/j.tins.2021.02.003> •

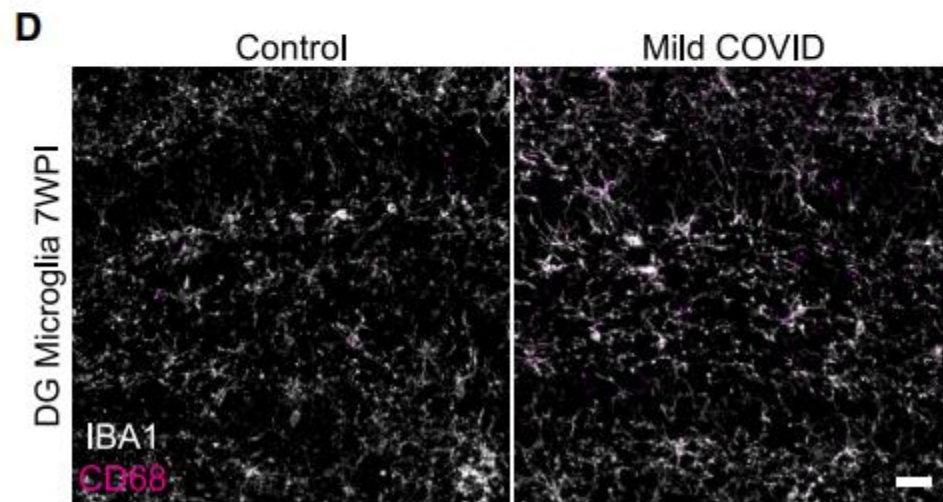
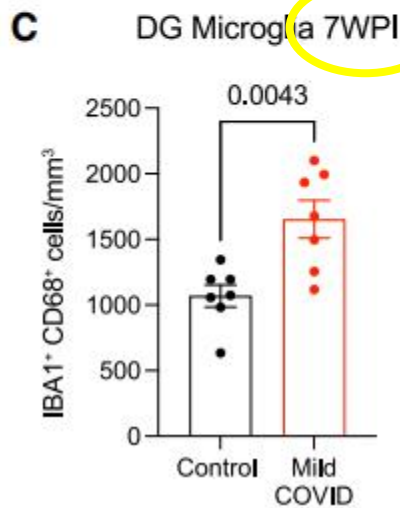
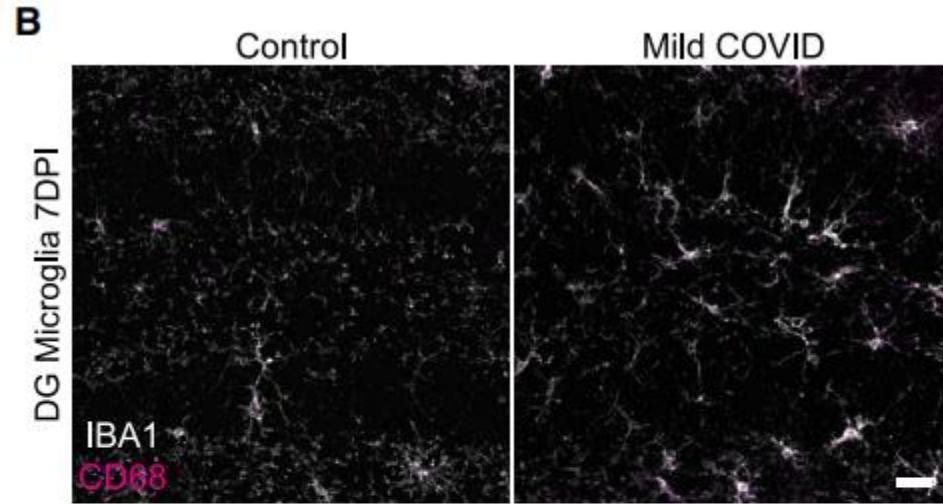
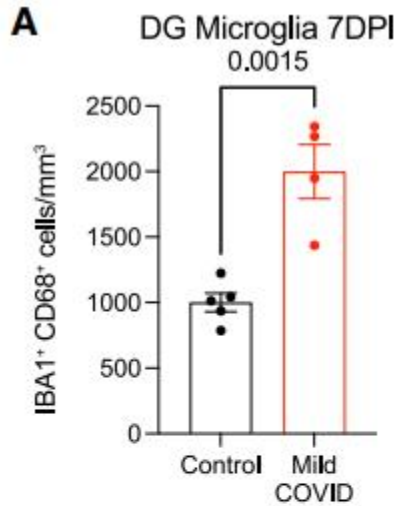
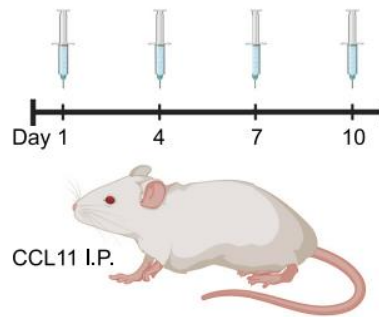


Il **chemobrain** (o deterioramento cognitivo correlato alla terapia del cancro, CRCI), è una condizione neuroinfiammatoria che i pazienti spesso sperimentano in seguito a radiazioni o chemioterapia.

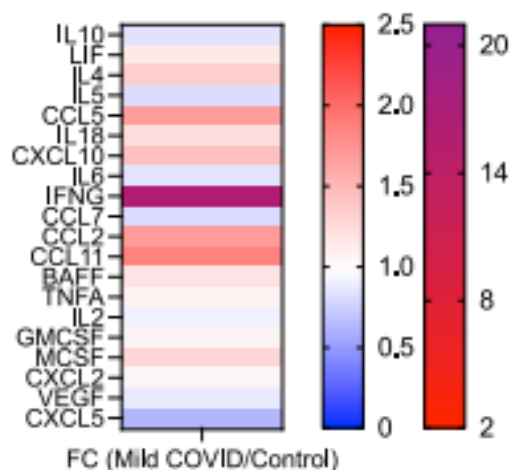
citochine neurotossiche e microglia reattiva



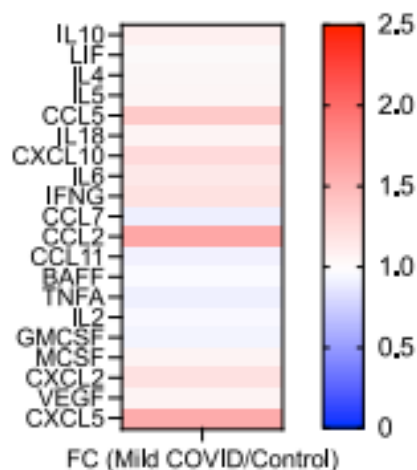
Cascata di eventi multicellulari



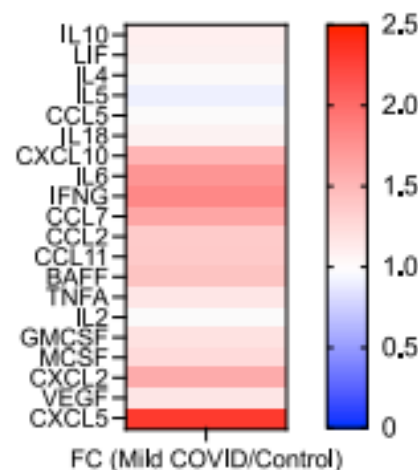
Serum Cytokines 7DPI



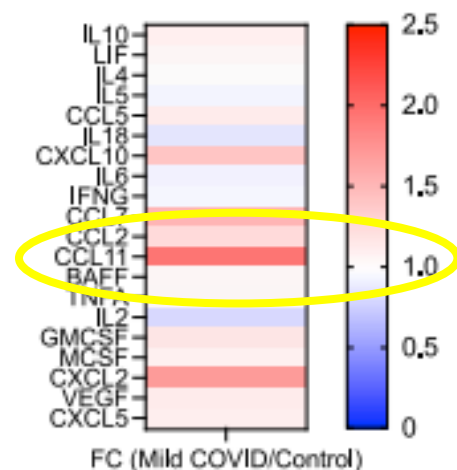
Serum Cytokines 7WPI

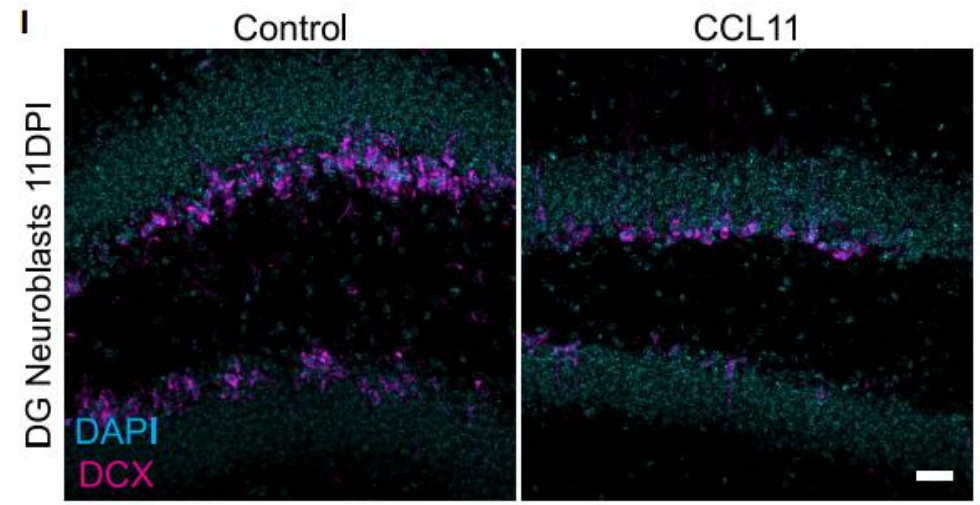
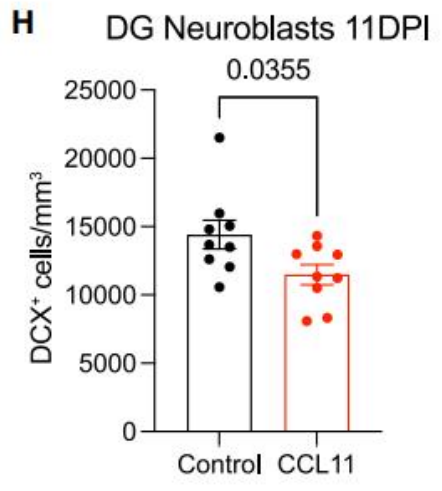
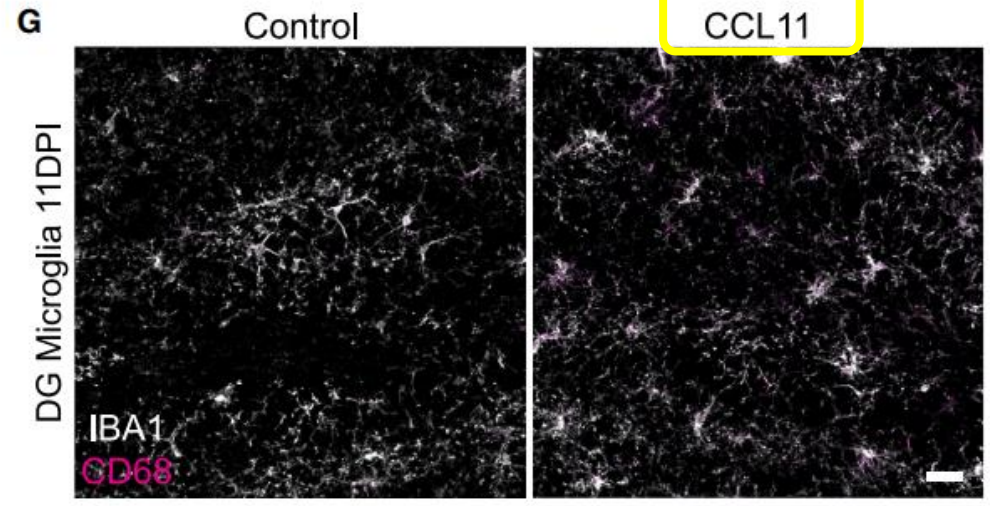
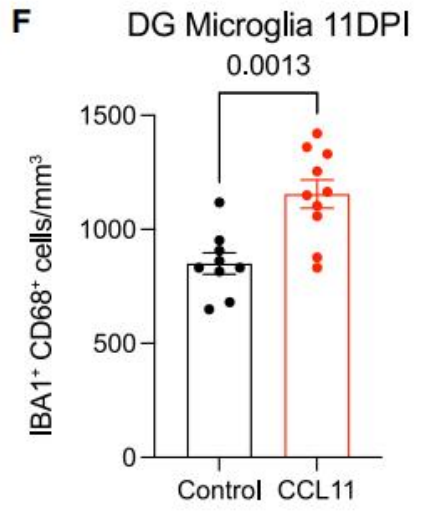
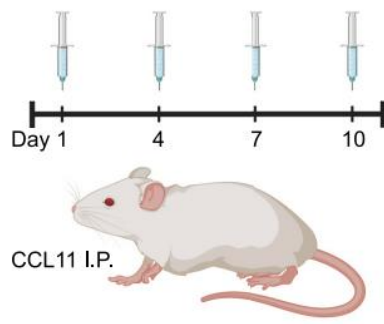


CSF Cytokines 7DPI



CSF Cytokines 7WPI






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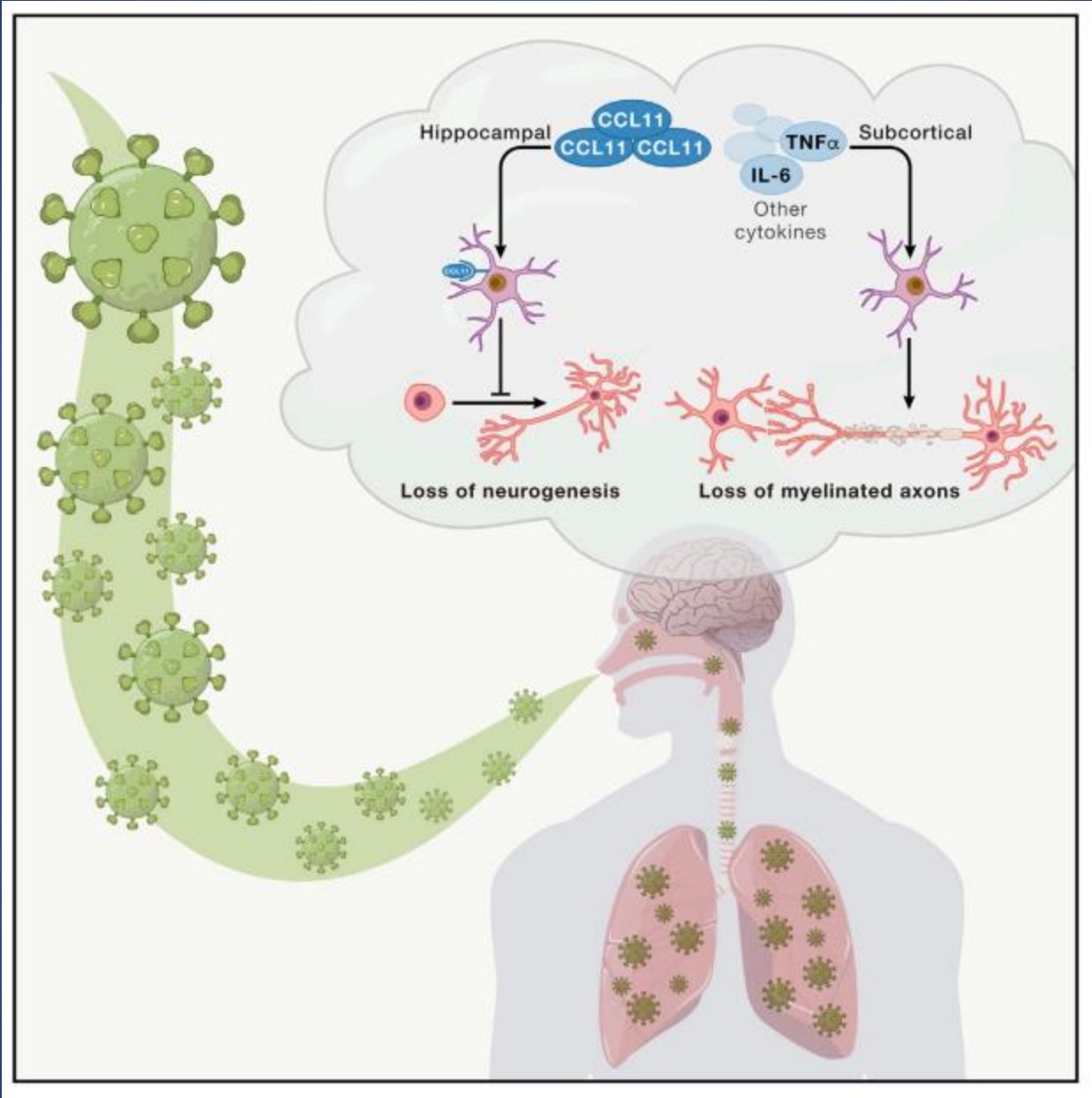
[Published: 31 August 2011](#)

The ageing systemic milieu negatively regulates neurogenesis and cognitive function

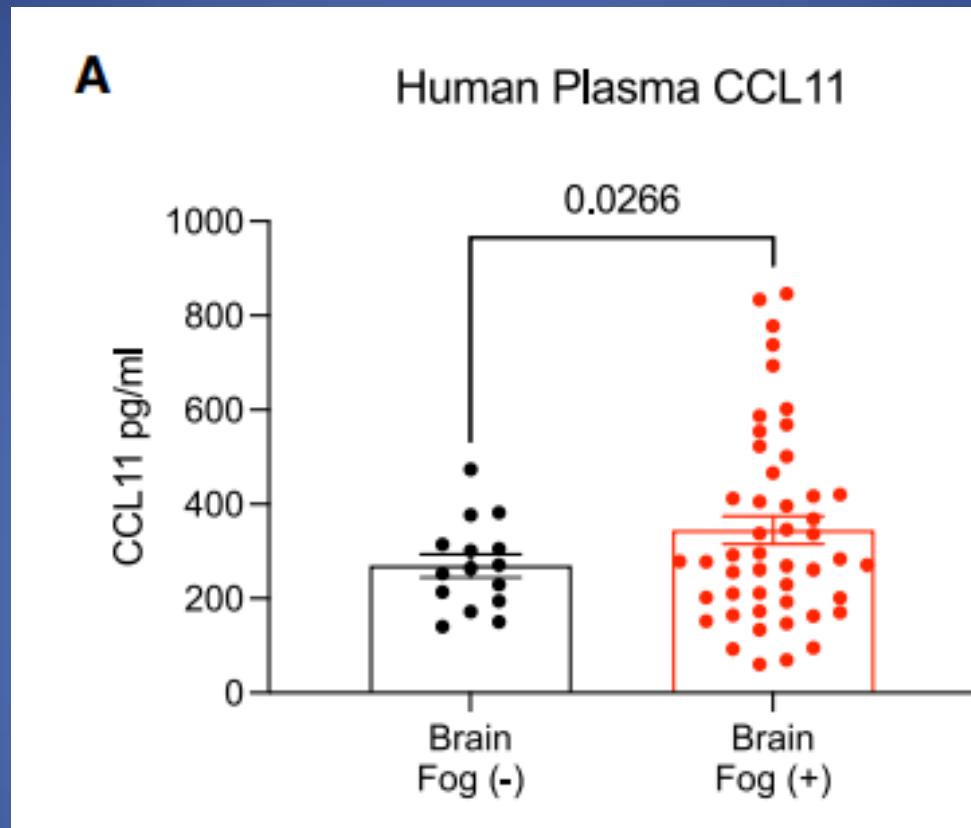
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Nature **477**, 90–94 (2011) | [Cite this article](#)

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Elevated CCL11 levels associated with cognitive impairment induce hippocampal dysregulation



(A) Plasma levels of CCL11 in people experiencing long COVID with (n = 48 human subjects, brain fog [+]) and without (n = 15 human subjects, brain fog [-]) cognitive symptoms.

DOI: 10.1126/SCIENCE.1088417 • Corpus ID: 36806485

Inflammatory Blockade Restores Adult Hippocampal Neurogenesis

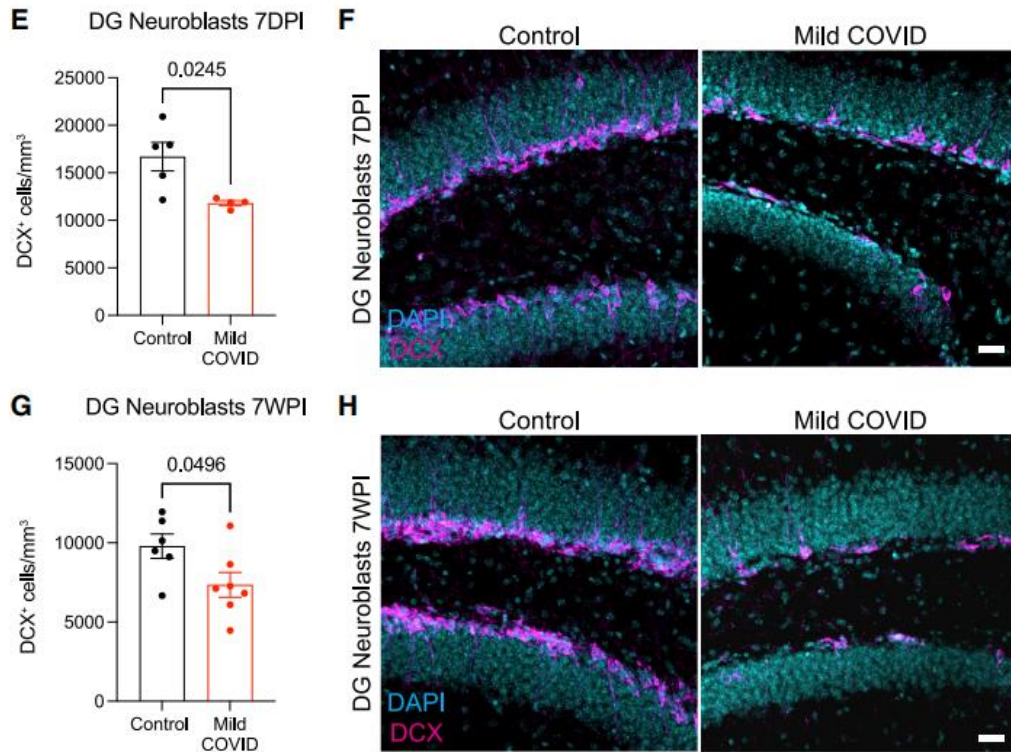
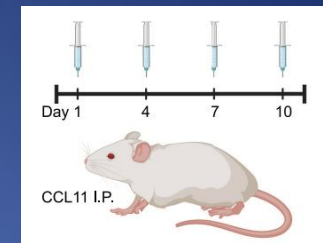
M. Monje, H. Toda, T. Palmer • Published 5 December 2003 • Biology, Medicine • Science

Cranial radiation therapy causes a progressive decline in cognitive function that is linked to impaired neurogenesis. Chronic inflammation accompanies radiation injury, suggesting that inflammatory processes may contribute to neural stem cell dysfunction. Here, we show that neuroinflammation alone inhibits neurogenesis and that inflammatory blockade with indomethacin, a common nonsteroidal anti-inflammatory drug, restores neurogenesis after endotoxin-induced inflammation and augments neurogenesis after cranial irradiation. [Collapse](#)

Differenziazione delle cellule progenitrici neuronali in nuove cellule



Figure 4. Decreased hippocampal neurogenesis after mild respiratory COVID



Il numero di nuovi neuroni era ridotto nei topi infetti e che questa riduzione era correlata al valore di microglia reattiva nell'ippocampo

La somministrazione sistemica di CCL11 ha riprodotto questo stesso schema nei topi non infetti

ARTICLE | VOLUME 103, ISSUE 2, P250-265.E8, JULY 17, 2019

Loss of Adaptive Myelination Contributes to Methotrexate Chemotherapy-Related Cognitive Impairment

Anna C. Geraghty • Erin M. Gibson • Reem A. Ghanem • ... Michael E. Greenberg • Frank M. Longo • Michelle Monje   • [Show all authors](#) • [Show footnotes](#)

[Open Archive](#) • Published: May 20, 2019 • DOI: <https://doi.org/10.1016/j.neuron.2019.04.032>

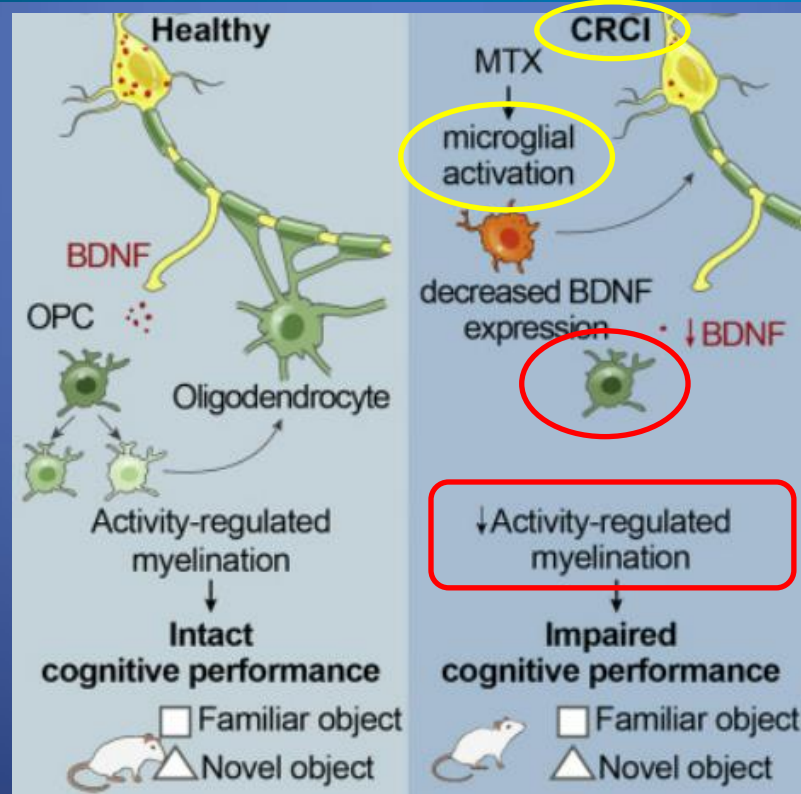
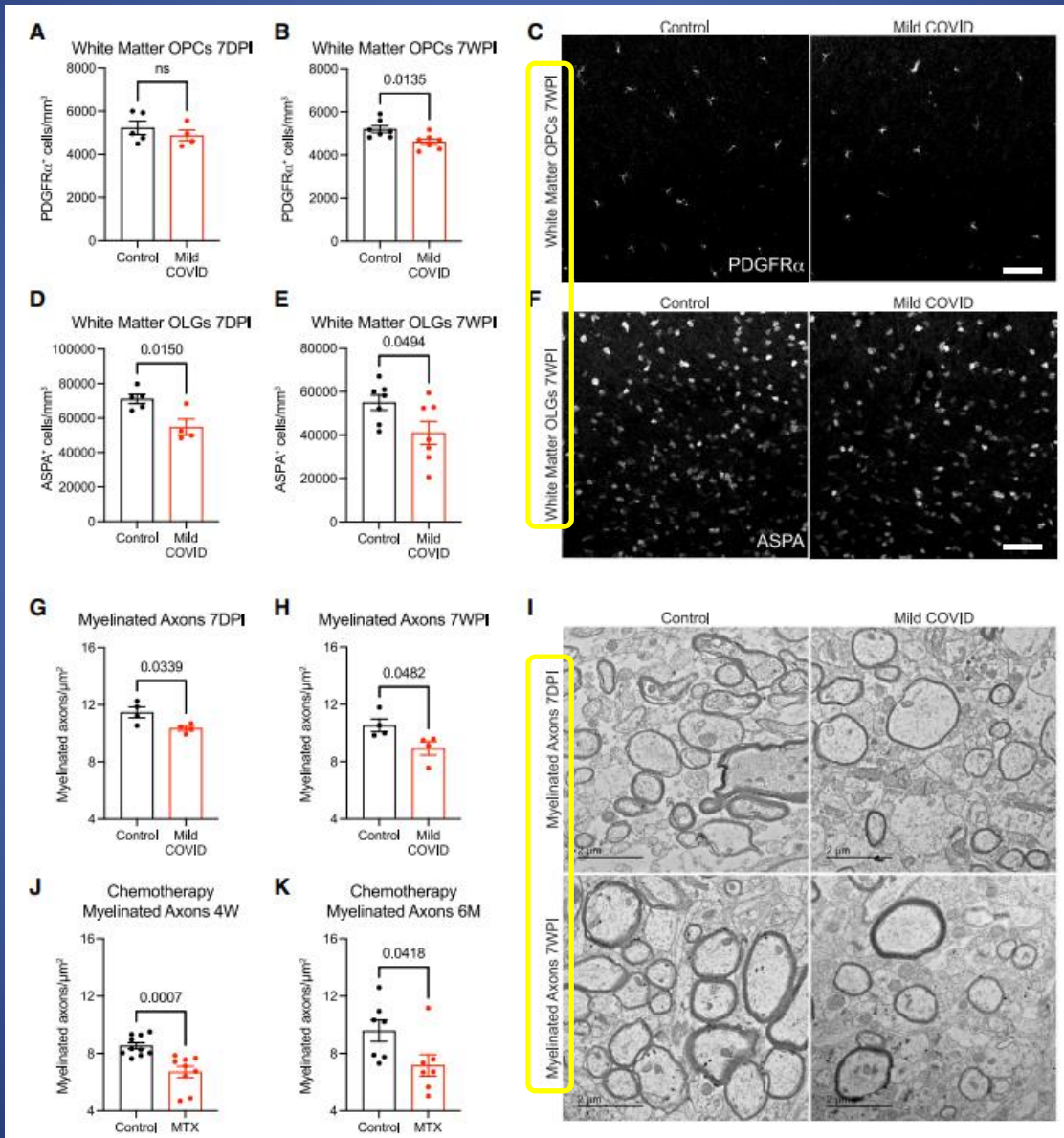
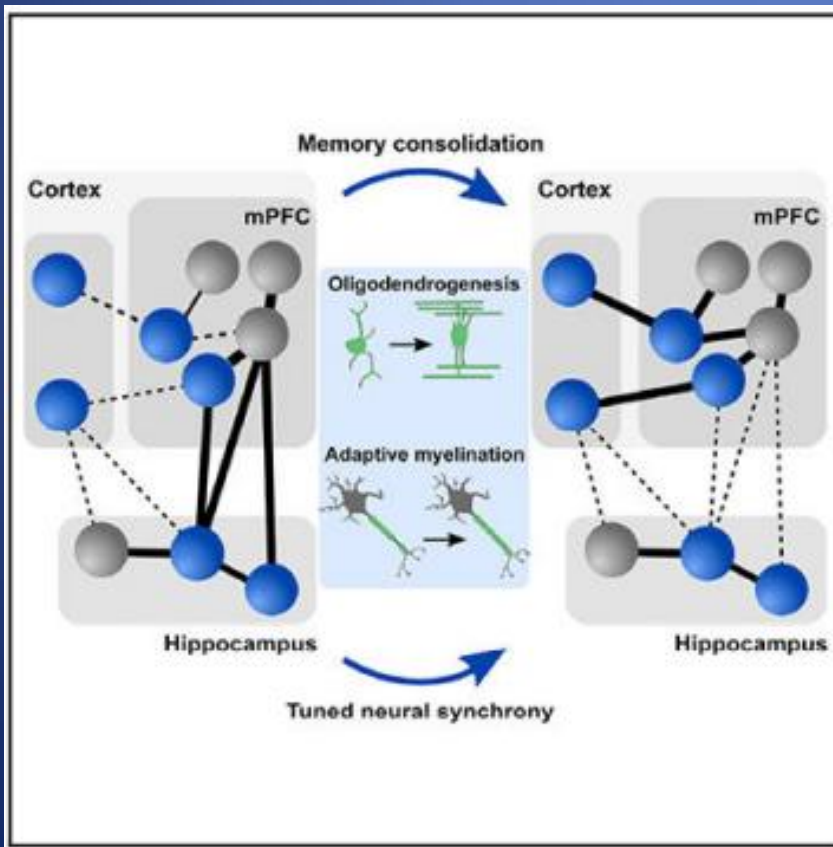


Figure 6. Oligodendrocyte and myelin loss after mild respiratory COVID



Disruption of Oligodendrogenesis Impairs Memory Consolidation in Adult Mice

Patrick E. Steadman^{1,2}, Frances Xia^{1,3}, Moriam Ahmed¹, Andrew J. Mocle^{1,3}, Amber R.A. Penning¹, Anna C. Geraghty⁴, Hendrik W. Steenland^{1,5}, Michelle Monje⁴, Sheena A. Josselyn^{1,2,3,6,7}, Paul W. Frankland^{1,2,3,6,8,9,*}



Inflammation



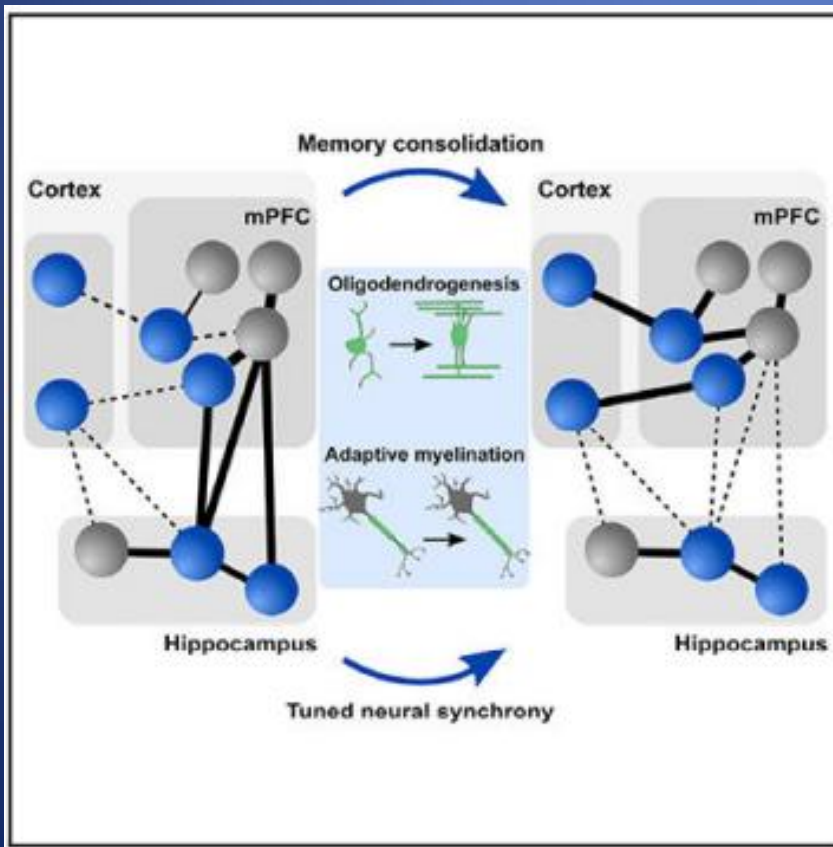
Disregolazione gliale



Circuiti neuronali

Disruption of Oligodendrogenesis Impairs Memory Consolidation in Adult Mice

Patrick E. Steadman^{1,2}, Frances Xia^{1,3}, Moriam Ahmed¹, Andrew J. Mocle^{1,3}, Amber R.A. Penning¹, Anna C. Geraghty⁴, Hendrik W. Steenland^{1,5}, Michelle Monje⁴, Sheena A. Josselyn^{1,2,3,6,7}, Paul W. Frankland^{1,2,3,6,8,9,*}



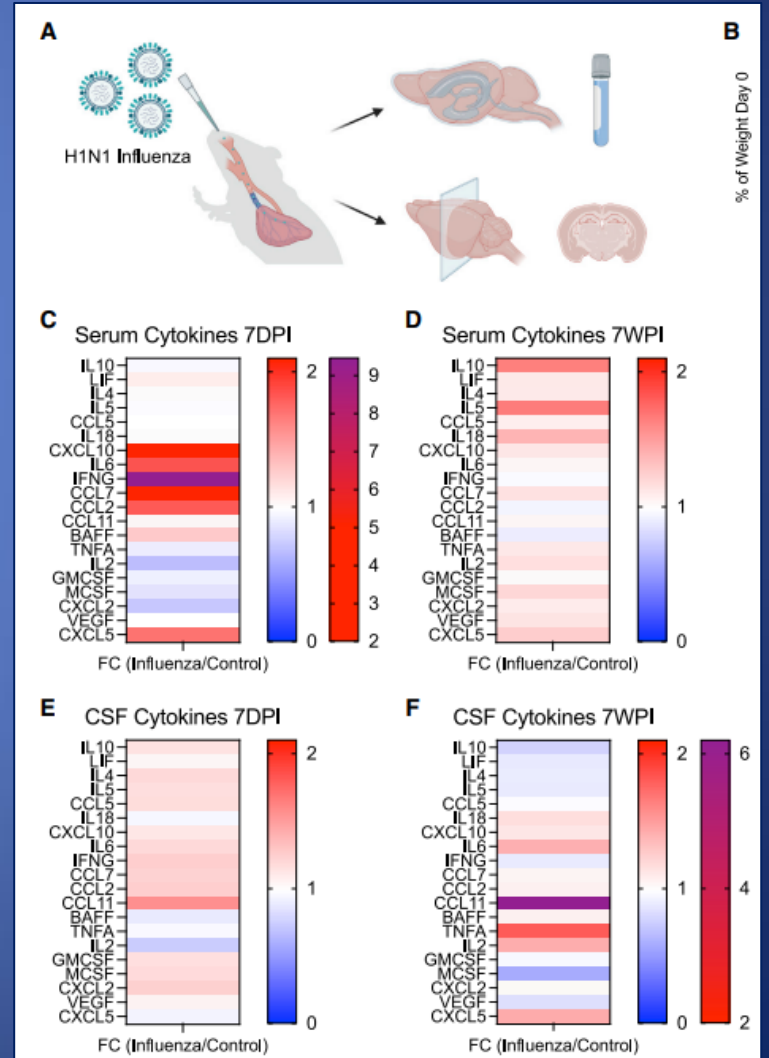
CCL11

persistentemente
elevata nell'infezione
H1N1
«influenza spagnola»

“An inexpressible dread”: psychoses of influenza at fin-de-siècle

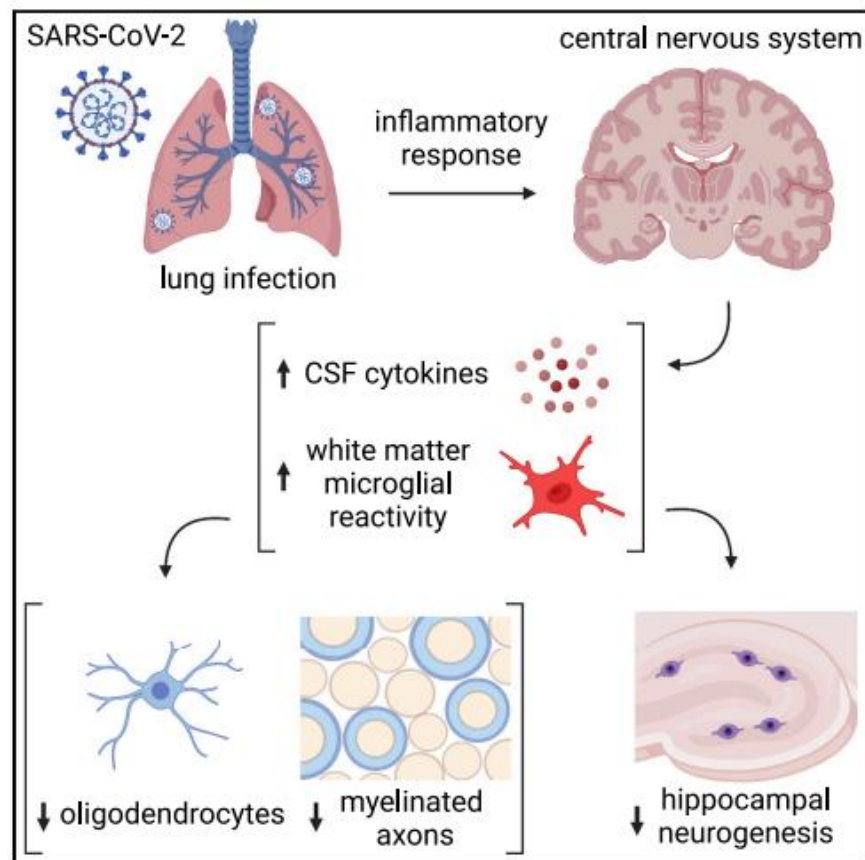
Mark Honigsbaum 

Published: March 23, 2013 • DOI: [https://doi.org/10.1016/S0140-6736\(13\)60701-1](https://doi.org/10.1016/S0140-6736(13)60701-1)



Mild respiratory COVID can cause multi-lineage neural cell and myelin dysregulation

Graphical abstract



Highlights

- Respiratory COVID induces CSF cytokine elevation and microglial reactivity
- CCL11 activates hippocampal microglia and impairs neurogenesis
- Respiratory COVID causes persistent loss of oligodendrocytes and myelinated axons
- Respiratory influenza causes similar but less persistent cellular dysregulation

In brief

Mild respiratory COVID causes neuroinflammation and multi-lineage cellular dysregulation in the central nervous system, a phenomenon mirroring cancer-therapy-related cognitive impairment.

San Martino

*La nebbia agl'irti colli,
piovigginando sale,
e sotto il maestrale,
urla e biancheggia il mar;
ma per le vie del borgo,
dal ribollir de' tini,
va l'aspro odor dè i vini,
l'anime a rallegrar.*

*Gira su ceppi accesi,
lo spiedo scoppiettando:
sta il cacciator fischando,
su l'uscio a rimirar.*

*tra le rossastre nubi,
stormi d'uccelli neri,
com'esuli pensieri,
nel vespero migrar.*

Giosuè Carducci

