



Relevant Neuropsychological Aspects in HIV Population in the COVID-19 Era

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Disclosure

Dr. Jose A. Muñoz-Moreno

October 2020

- Dr. Muñoz-Moreno has received **speaker honoraria** from Gilead Sciences.
- No other conflicts of interest.



1. Neuropsychology and HIV: Rapid Update

2. Impact of COVID-19 on Neuropsychological Status

3. Relevant Practical Considerations



1. Neuropsychology and HIV: Rapid Update

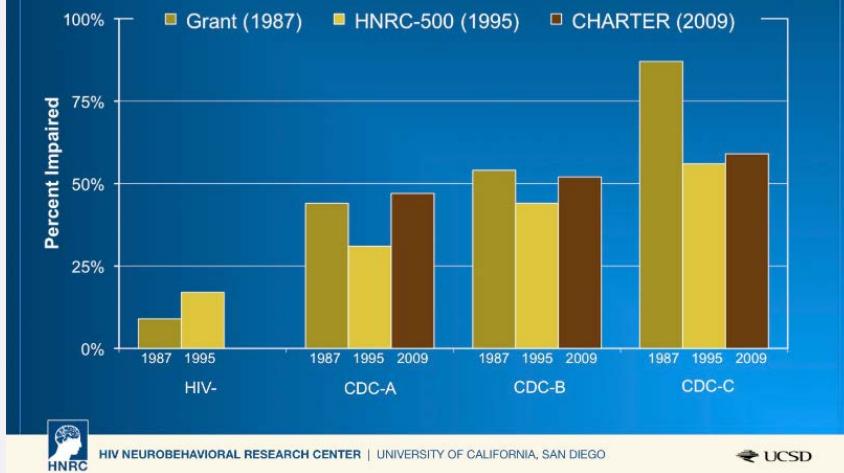


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Neuropsychology and HIV: Rapid Update

👉 Current HAND Progression?

Although combination ARVs improve health and prolong survival, neuroAIDS remains prevalent



Grant et al, CROI, 2009

?

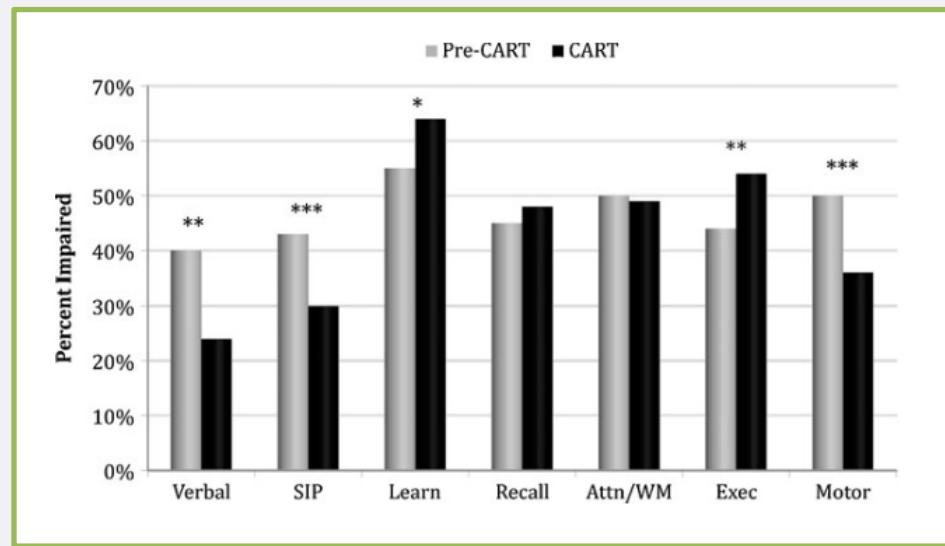


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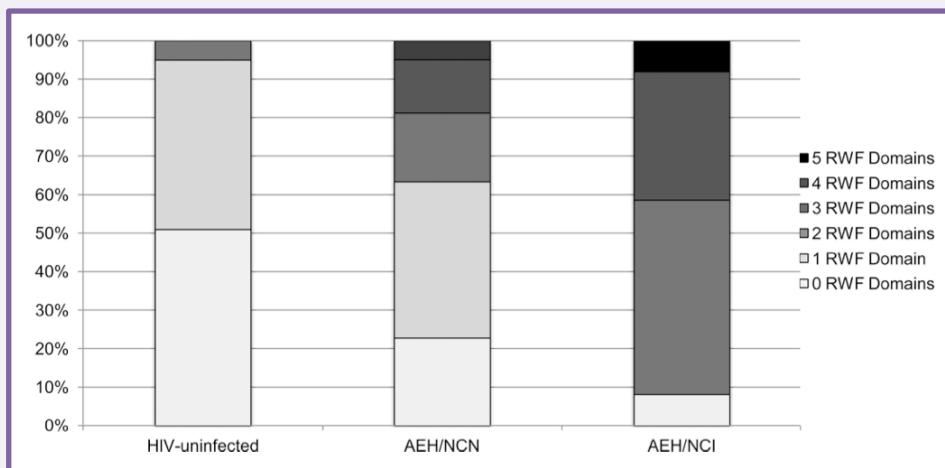
Neuropsychology and HIV: Rapid Update

👉 Current HAND Progression?

👉 Variable Impairment Pattern + Functional Decline



Heaton et al, J Neurovirol, 2011



AEH, Acute/early infection; NCN, Neurocognitive normal;
NCI, Neurocognitive impairment; RWF, Real-world function

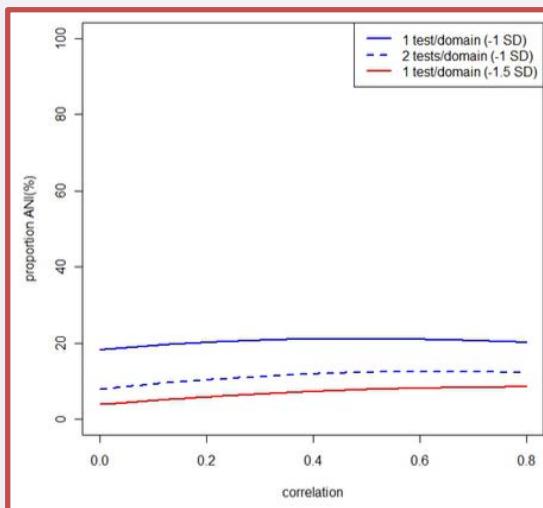
Doyle et al, J Neurovirol, 2013



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Neuropsychology and HIV: Rapid Update

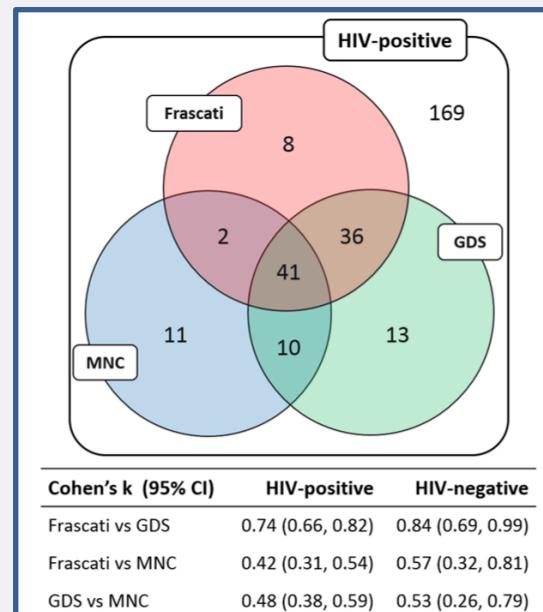
👉 Current HAND Progression?



Gisslén et al,
BMC Infect Dis, 2011

👉 Variable Impairment Pattern +
Functional Decline

👉 Methodological Issues



De Francesco et al,
BMC Infect Dis, 2016



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Neuropsychology and HIV: Rapid Update

👉 **Current HAND Progression?**

👉 **Variable Impairment Pattern + Functional Decline**

👉 **Methodological Issues**

👉 **Chronicity, Aging, and Multiple Risk Factors**

Disease factors	Low nadir CD4 ⁺ T-cell count High plasma HIV RNA; high CSF HIV RNA Low current CD4 (pre-cART) Presence of past HIV-related CNS diseases Longer HIV duration
Treatment factors	Low cART adherence Episodes of cART interruption Nonoptimal cART regimen Short cART duration (related to treatment failure)
Comorbidities	Positive HCV serostatus with high HCV RNA History of acute CV event CV risk factors (hyperlipidemia, elevated blood pressure, chronic diabetes, and diabetes type II) Anemia and thrombocytopenia
Demographic factors	Older age Low level of educational achievement Ethnicity Sex (female, as associated with lower socioeconomic status in some countries) Lack of access to standard care; poverty

*Mind Exchange Group,
CID, 2013*

Vascular cognitive impairment and HIV-associated neurocognitive disorder: a new paradigm

Lucette A. Cysique ^{1,2,3}  • Bruce J. Brew ^{2,3,4,5}

Cysique et al, J Neurovirol, 2019



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Neuropsychology and HIV: Rapid Update

👉 Current HAND Progression?



👉 Variable Impairment Pattern + Functional Decline

👉 Methodological Issues

👉 Chronicity, Aging, and Multiple Risk Factors

👉 ART Neurotoxicity?

CLINICAL SCIENCE

Antiretroviral drug concentrations in brain tissue of adult decedents

Ferrara, Micol^a; Bumpus, Namandjé N.^b; Ma, Qing^c; Ellis, Ronald J.^d; Soontornniyomkij, Virawudh^d; Fields, Jerel A.^d; Bharti, Ajay^d; Achim, Cristian L.^d; Moore, David J.^d; Letendre, Scott L.^d

[Author Information](#) ⓘ

AIDS: November 01, 2020 - Volume 34 - Issue 13 - p 1907-1914

doi: 10.1097/QAD.0000000000002628

- *N=11. First analyses in brain tissue.*
- *Wide variability and higher concentrations (TDF, EFV, LPV).*
- *Association with worse cognitive functioning.*



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2. Impact of COVID-19 on Neuropsychological Status



**COVID-19
Infection**

vs

Pandemic



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**COVID-19
Infection**

vs

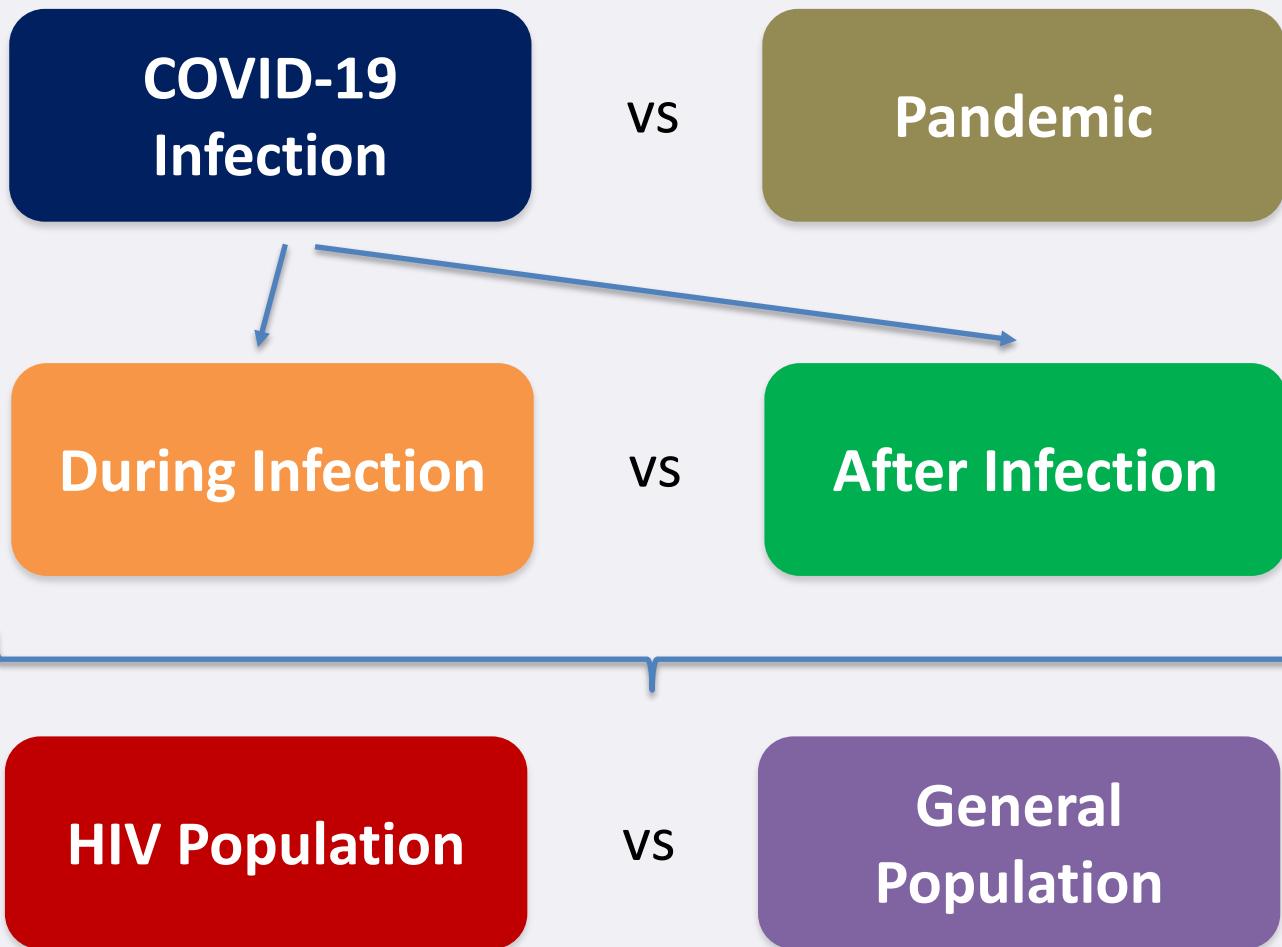
Pandemic

During Infection

vs

After Infection





COVID-19 Infection



During Infection

HIV Population





*"Neuropsychological" / "Cognitive"
"SARS-CoV-2" / "COVID-19"
"HIV"*

October 12th

NO RESULTS



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PubMed.gov

*"Neurologic" / "Brain"
"SARS-CoV-2" / "COVID-19"
"HIV"*

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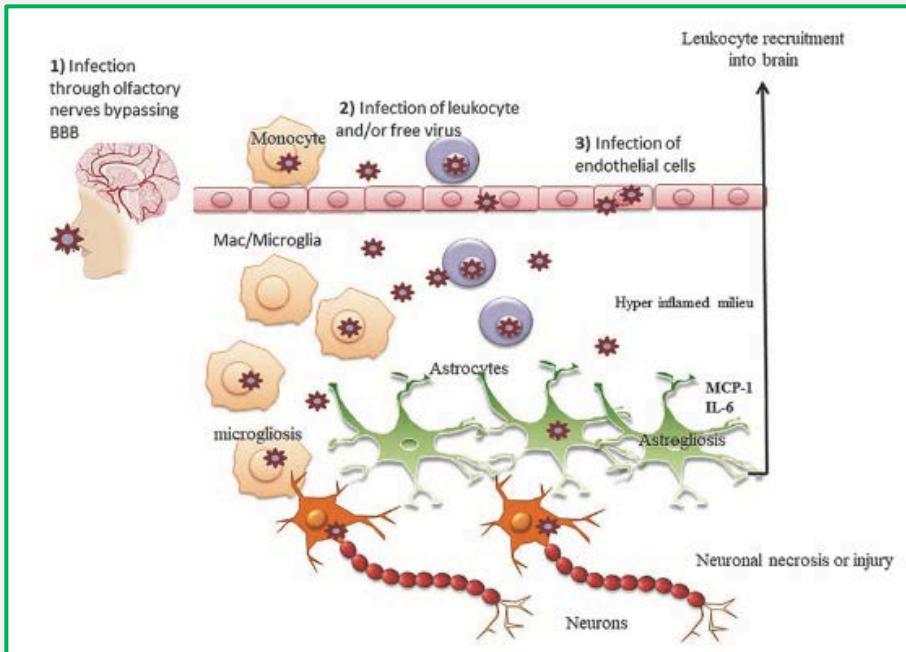
1 RESULT



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What HIV in the Brain Can Teach Us About SARS-CoV-2 Neurological Complications?

Lena Al-Harthi ¹, Edward Campbell ², Julie A Schneider ³, David A Bennett ³



- Non-systematic review.
- Poorly understood spectrum of COVID-19-related neurologic symptoms.
- Potentially similar mechanisms to affect the CNS compared with HIV infection.

COVID-19 Infection



During Infection

General
Population



"Neuropsychological" / "Cognitive" "SARS-CoV-2" / "COVID-19"

October 12th

54 results



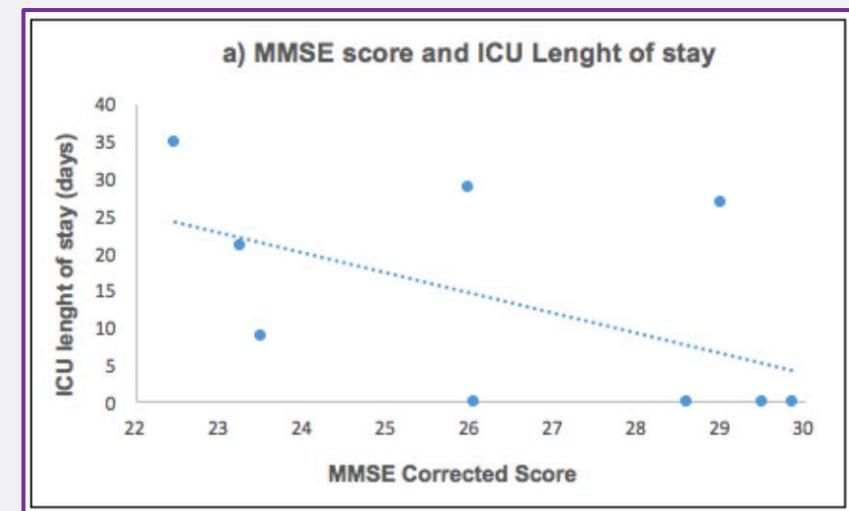
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> Arch Phys Med Rehabil. 2020 Sep 26;S0003-9993(20)30961-8.
doi: 10.1016/j.apmr.2020.09.376. Online ahead of print.

Neuropsychological features of severe hospitalized COVID-19 patients at clinical stability and clues for post-acute rehabilitation

Francesco Negrini ¹, Irene Ferrario ², Daniele Mazziotti ¹, Marzia Berchicci ¹, Maurizio Bonazzi ¹, Alessandro de Sire ³, Stefano Negrini ⁴, Laura Zapparoli ⁵

- N=9, >30 days after hospital admission, no cognitive symptoms before hospitalization.
- 3 of 9 (33%) presented impairment by MMSE. Not associated with emotional status.
- Association with days in the ICU ($p=??$).





Collection: Databases of international organizations

Database: WHO COVID

Type: Article

Journal: European Journal of Neurology

Clinical aspect: Etiology

Year: 2020

COVID-19 related mortality in patients with cognitive impairment: A Hospital-based retrospective cohort study

Seoane, D.; Roca-Rodríguez, L.; Muñoz-García, M. I.; Martín-Jiménez, P.; García-Reyne, A.; Laluez, A.; Maestro, G.; Folgueira, D.; Blanco-Palmero, V. A.; Herrero-San Martín, A.; Llamas-Velasco, S.; Pérez-Martínez, D. A.; González-Sánchez, M.; Villarejo-Galende, A..

European Journal of Neurology; 27:1307, 2020.

Article | WHO COVID | ID: covidwho-708994

- 281 deceased by COVID-19 vs 138 deceased by other causes.
- Presence of cognitive impairment in COVID-19 patients: 9%.
(72% dementia, 28% mild cognitive impairment)
- Older, living in nursing homes, and shorter time from symptoms onset to death.



Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic

Jonathan P Rogers*, Edward Chesney*, Dominic Oliver, Thomas A Pollak, Philip McGuire, Paolo Fusar-Poli, Michael S Zandi, Glyn Lewis, Anthony S David

www.thelancet.com/psychiatry Published online May 18, 2020

- Systematic review:
72 studies.
- Until April 10th.
- Included acute and post symptoms.
- Symptoms during infection:
Insomnia, anxiety, impaired attention, impaired memory, and depressed mood.

	Acute			
	Studies	Cases	Sample size	Prevalence (95% CI)
Any	1	17	27	63·0% (43·8-80·4)
Insomnia	2	54	129	41·9% (22·5-50·5)
Anxiety	2	46	129	35·7% (27·6-44·2)
Impaired concentration or attention	1	39	102	38·2% (29·0-47·9)
Impaired memory	2	44	129	34·1% (26·2-42·5)
Depressed mood	2	42	129	32·6% (24·7-40·9)
Confusion	2	36	129	27·9% (20·5-36·0)
Emotional lability	1	30	102	29·4% (0·4-7·3)
Altered consciousness	1	17	82	20·7% (12·6-30·3)
Pressured speech	1	21	102	20·6% (13·3-29·0)
Euphoria	1	8	102	7·8% (3·3-14·0)



Correlation between immune response and self-reported depression during convalescence from COVID-19

Bo Yuan ¹, Weixin Li ², Hanqing Liu ³, Xin Cai ¹, Shuo Song ³, Jia Zhao ³, Xiaopeng Hu ³, Zhiwen Li ³, Yongxin Chen ², Kai Zhang ⁴, Zhiyong Liu ⁴, Jing Peng ⁴, Cheng Wang ², Jianchun Wang ⁵, Yawen An ⁶

- High rate of self-reported depression (44%), N=96.
- Immune factors related to depression.
- Bidirectional connection between depression and inflammation.

Table 2
Comparison of immune factors in COVID-19 discharged patients.

Immune factors	Reference range	Normal group	Self-reported Depression	P value
WBC ($10^9/L$)	3.5–9.5	6.0 \pm 1.5	6.7 \pm 1.5*↑	0.016
NEUT ($10^9/L$)	1.8–6.3	3.3 \pm 0.9	4.1 \pm 1.2***↑	0.000
LYM ($10^9/L$)	1.1–3.2	1.9 \pm 0.6	1.8 \pm 0.5	0.468
MON ($10^9/L$)	0.1–0.6	0.5 \pm 0.2	0.5 \pm 0.2	0.744
EOS ($10^9/L$)	0.02–0.52	0.1 \pm 0.1	0.1 \pm 0.1	0.568
BASO ($10^9/L$)	0–0.06	0.0 \pm 0.0	0.0 \pm 0.0	0.800
Neutrophil-to-Lymphocyte Ratio (NLR)	/	1.8 \pm 0.6	2.4 \pm 0.9***↑	0.000
NEUT ratio (%)	40–75	55.7 \pm 6.4	61.0 \pm 7.1***↑	0.000
LYM ratio (%)	20–50	32.3 \pm 6.3	28.1 \pm 6.7**↓	0.002
BASO ratio (%)	0–1	0.7 \pm 0.3	0.6 \pm 0.3	0.107
EOS ratio (%)	0.4–8.0	2.2 \pm 1.5	2.1 \pm 1.4	0.741
MONO ratio (%)	3–10	9.0 \pm 2.4	8.2 \pm 2.6	0.148
HS-CRP (mg/dL)	0–0.5	0.1 \pm 0.1	0.2 \pm 0.3*↑	0.035
IL-6 (pg/mL)	1.5–5000	56.1 \pm 105.3	40.7 \pm 65.6	0.518



*"Neurologic" / "Brain" / "CNS"
"SARS-CoV-2" / COVID-19*

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☞ Title:

190 results

☞ Abstract:

1,598 results



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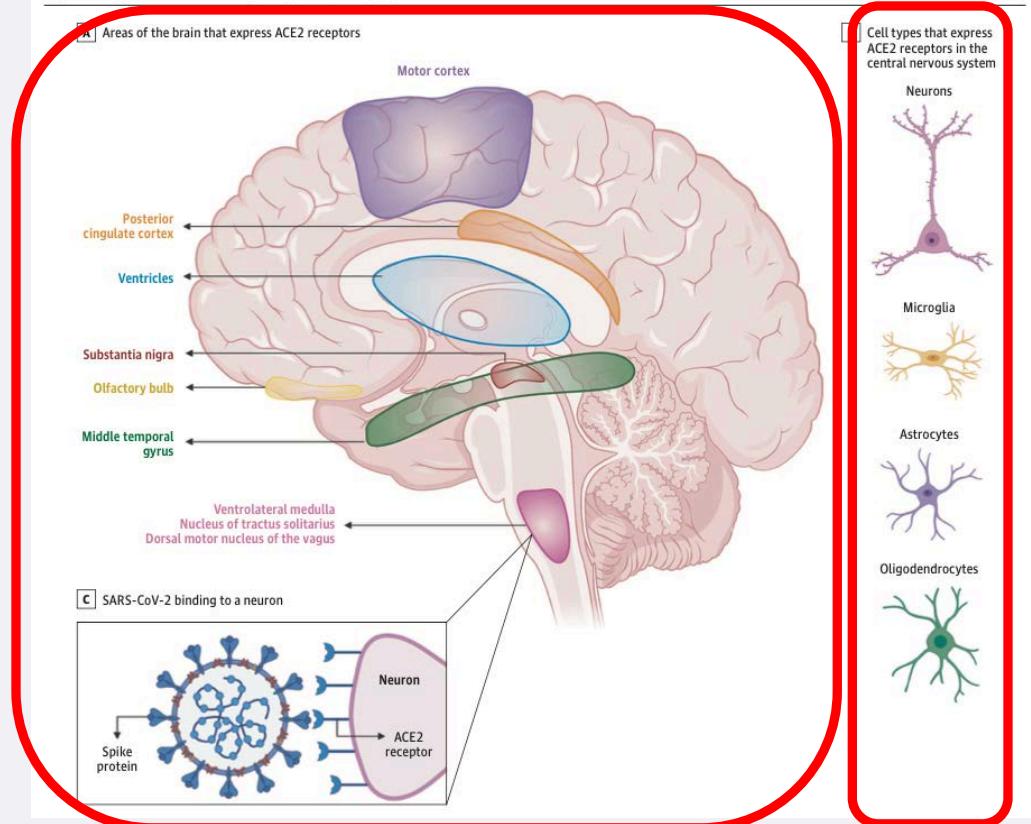
Neuropathogenesis and Neurologic Manifestations of the Coronaviruses in the Age of Coronavirus Disease 2019 A Review

Adeel S. Zubair, MD; Lindsay S. McAlpine, MD; Tova Gardin, MD, MPP; Shelli Farhadian, MD, PhD; Deena E. Kuruvilla, MD; Serena Spudich, MD

JAMA Neurology August 2020 Volume 77, Number 8

➤ ACE2 receptors

Figure 1. Angiotensin-Converting Enzyme 2 (ACE2) Expression in the Brain



**COVID-19
Infection**

After Infection

HIV Population





*"Neuropsychological" / "Cognitive"
"SARS-CoV-2" / "COVID-19"
"HIV"*

October 12th

NO RESULTS



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**COVID-19
Infection**

After Infection

**General
Population**



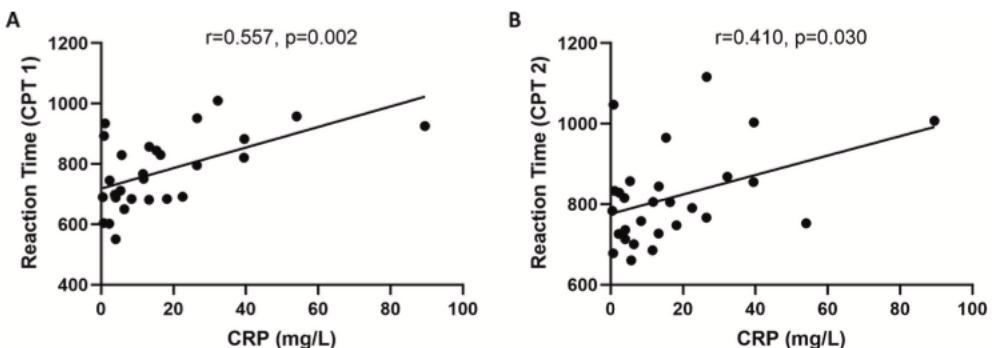
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The landscape of cognitive function in recovered COVID-19 patients

Hetong Zhou ¹, Shaojia Lu ¹, Jingkai Chen ¹, Ning Wei ¹, Dandan Wang ¹, Hailong Lyu ¹, Chuan Shi ², Shaohua Hu ³

COVID-19
n=29

Controls
n=29



- Worse performance in attention/concentration (CPT: 3 tasks).
- Association with inflammation markers (CRP).

Results of neuropsychological tests in all participants.

Measure	COVID-19 patients (N = 29)	Controls (N = 29)	t	p
Trail Making Test	47.82 ± 16.55	49.76 ± 21.53	-0.383	0.703
Sign Coding Test	32.14 ± 9.02	34.48 ± 13.31	-0.784	0.432
Digital Span Test	19.24 ± 5.36	18.97 ± 5.23	0.198	0.843
Continuous Performance Test				
CPT part 1				
Correct Number	9.83 ± 1.93	10.21 ± 2.62	-0.627	0.533
Error Number	0.41 ± 0.63	0.97 ± 2.61	-1.106	0.273
Missing Number	39.76 ± 1.96	38.83 ± 3.56	1.235	0.222
Reaction time	774.59 ± 119.33	843.22 ± 140.97	-2.001	0.050
CPT part 2				
Correct Number	7.07 ± 2.45	8.72 ± 1.79	-2.938	0.050
Error Number	1.38 ± 1.59	1.66 ± 2.19	-0.549	0.586
Missing Number	41.55 ± 2.90	39.59 ± 2.31	2.857	0.006*
Reaction time	817.06 ± 114.53	879.59 ± 123.87	-1.996	0.051
CPT part 3				
Correct Number	6.34 ± 2.50	8.21 ± 1.90	-3.198	0.002*
Error Number	3.28 ± 1.85	3.34 ± 2.32	-0.125	0.901
Missing Number	40.38 ± 3.10	38.45 ± 2.13	2.765	0.008*
Reaction time	868.24 ± 99.73	879.10 ± 197.08	-0.265	0.792

Review

> J Neurovirol.

2020 Sep 3;1-15. doi: 10.1007/s13365-020-00897-2.

Online ahead of print.

Studying the neuropsychological sequelae of SARS-CoV-2: lessons learned from 35 years of neuroHIV research

Andrew Levine ¹, Ned Sacktor ², James T Becker ³

- Experience from 35 years of research in NeuroAIDS field.
- Necessity of large cohorts, including infected and recovered people, and never-infected.
- Also relevant trans-cultural issues, as well as international collaborations.



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Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic

Jonathan P Rogers*, Edward Chesney*, Dominic Oliver, Thomas A Pollak, Philip McGuire, Paolo Fusar-Poli, Michael S Zandi, Glyn Lewis, Anthony S David

www.thelancet.com/psychiatry Published online May 18, 2020

► Main persisting symptoms:

Sleep disorder, frequent recall of memories, emotional lability, fatigue, impaired attention, and impaired memory.

	Post-illness			
	Studies	Cases	Sample size	Prevalence (95% CI)
Any	1	0	4	0 (0.0–39.1)
Insomnia	4	34	280	12.1% (8.6–16.3)
Anxiety	2	21	171	12.3% (7.7–17.7)
Impaired concentration or attention	2	34	171	19.9% (14.2–26.2)
Impaired memory	3	44	233	18.9% (14.1–24.2)
Depressed mood	5	35	332	10.5% (7.5–14.1)
Confusion	1	1	621	0.2% (0.0–0.7)
Emotional lability	1	24	102	23.5% (15.8–32.3)
Altered consciousness	NA	NA	NA	NA
Pressured speech	1	12	102	11.8% (6.1–18.8)
Euphoria	1	11	102	10.8% (5.4–17.6)
Aggression	1	1	102	1.0% (0.0–4.2)
Irritability	3	28	218	12.8% (8.7–17.6)
Auditory hallucinations	1	1	102	1.0% (0.0–4.2)
Persecutory ideas	1	2	102	2.0% (0.0–5.8)
Visual hallucinations	NA	NA	NA	NA
Suicidality	1	0	102	0 (0.0–1.7)
Fatigue	4	61	316	19.3% (15.1–23.9)
Frequent recall of traumatic memories	1	55	181	30.4% (23.9–37.3)
Sleep disorder	1	14	14	100% (88.0–100.0)
Psychotic symptoms (unspecified)	1	4	90	4.4% (1.0–9.9)
Self-harm	1	1	102	1.0% (0.0–4.2)

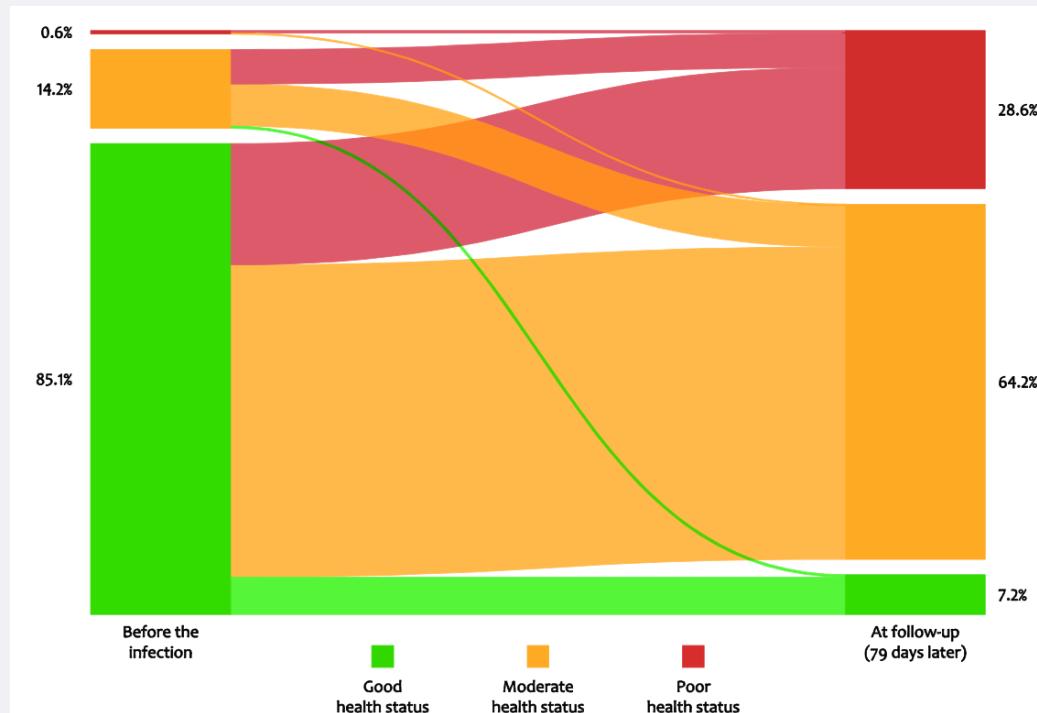




Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome?

Yvonne M.J. Goertz, Maarten Van Herck, Jeannet M. Delbressine, Anouk W. Vaes, Roy Meys, Felipe V.C. Machado, Sarah Houben-Wilke, Chris Burtin, Rein Posthuma, Frits M.E. Franssen, Nicole van Loon, Bita Hajian, Yvonne Spies, Herman Vijlbrief, Alex J. van 't Hul, Daisy J.A. Janssen, Martijn A. Spruit

ERJ Open Research 2020; DOI: 10.1183/23120541.00542-2020

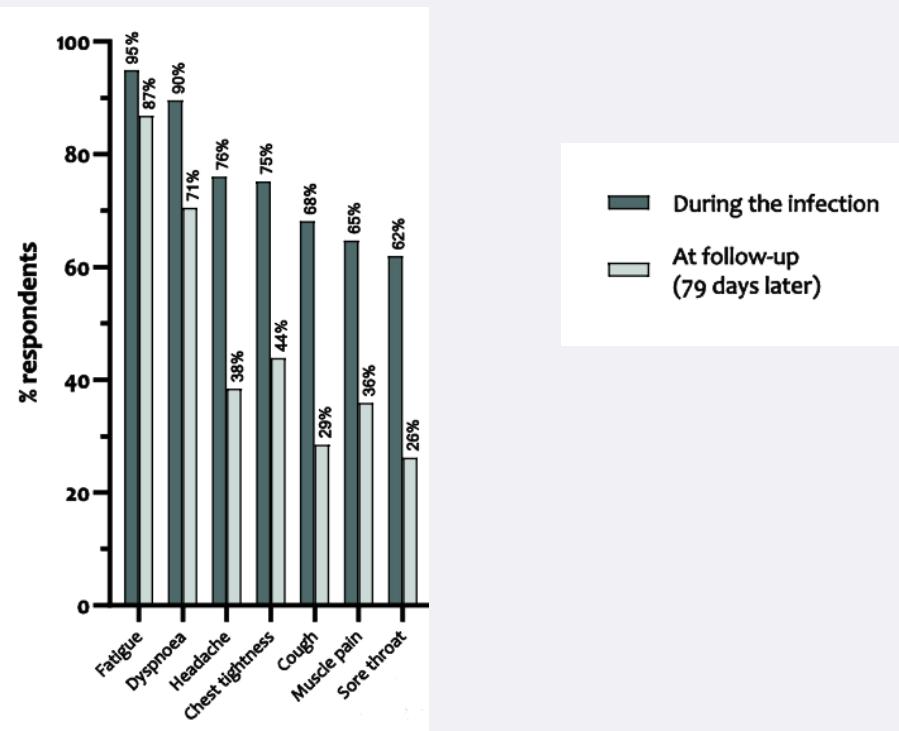




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ERJ Open Research 2020; DOI: 10.1183/23120541.00542-2020



NeuroCOVID-19 SIG

An increasing number of reports indicate that COVID-19 may be associated with neurocognitive symptoms, suggesting that rigorously conducted studies in COVID-19 patients are needed. The global aspect of the pandemic requires a global response in terms of cross-cultural validity of testing protocols with equal access to neurological care in mind. Of course, the socio-economic and health consequences of the infection require primary consideration, so that any neuroCOVID-19 investigations are perceived as an added necessity rather than an added burden in already maximally stretched healthcare systems.



ADDENDUM I: SIG MEMBERS.

Please enter the names and email addresses for members. The application requires at least 20, but you may list more. Ask each member to indicate the number of years of experience post-degree. Please check all boxes that apply for each member.

Name	Email Address	Years of post-degree experience	Current Postdoc	Current Student	Country
1. Emilia Łojek <emilia@psych.uw.edu.pl>		>15			Poland
2. Lucette Cysique <lcysique@unsw.edu.au>		>15			Australia
3. April Denise Thames <thames@usc.edu>		>5			USA
4. Jackie Hoare <hoare.iax@gmail.com>		>10			South Africa
5. Jose A. Muñoz-Moreno <jmuñoz@fsida.org>		>15			Spain
6. Maite Garolera <MGarolera@CST.CAT>		>15			Spain
7. Pariya Wheeler Fazeli <pifazeli@uab.edu>		>5			USA
8. Robert K Heaton <heaton@ucsd.edu.au>		>30			USA
9. Robert Paul <Robert.Paul@mimh.edu>		>20			USA
10. Sean Rourke <sean.rourke@utoronto.ca>		>20			Canada
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13. Robbins, Reuben <rnr2110@cumc.columbia.edu>		>15			USA
14. David Moore <dmoore@ucsd.edu.au>		>15			USA
15. john.joska@uct.ac.za <john.joska@uct.ac.za>		>15			South Africa

Pandemic

HIV Population

vs

General
Population



Global Characteristics of the Pandemic

Social Distancing

- Depression
- Anxiety
- Loneliness



Poor Access to Care

- Limited healthcare
- Access to therapies

Economical Impact

- Emotional status
- Socio-economical necessities
- Access to care

Worrying about Future

- Uncertainty
- End of the pandemic?



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I LES MALALTIES INFECCIOSES

Abstract: C-AIDS2020-10686



AN IAS VIRTUAL CONFERENCE | 10 - 11 JULY 2020

Psychosocial Impact of COVID-19: A Systematic Review. What Do We Know So Far?

Pere Torres-Bertral^{1,2}, Carmina R. Fumaz¹, Maria J. Ferrer Lasala¹, Bonaventura Clotet^{1,3,4}, Jose A. Muñoz-Moreno^{1,5}

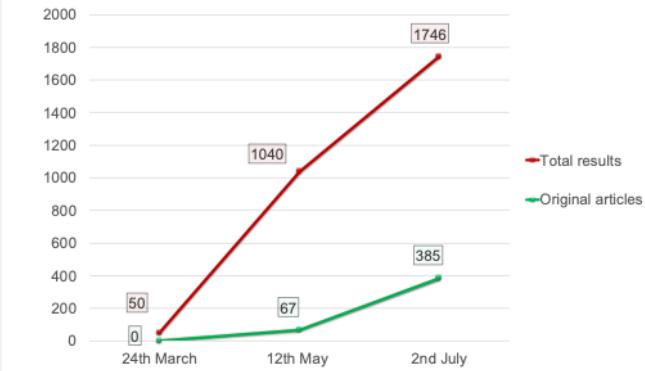
¹ Fundació Lluita contra la SIDA (FLS) – Infectious Diseases Department, Hospital Universitari Germans Trias i Pujol, Badalona, Catalonia, Spain / ² Institut Català d'Oncologia (ICO) – Hospital Universitari Germans Trias i Pujol, Badalona, Catalonia, Spain / ³ IrsiCaixa AIDS Research Institute - HIVACAT, Hospital Universitari Germans Trias i Pujol, Badalona, Catalonia, Spain / ⁴ Faculty of Medicine, Universitat de Vic - Universitat Central de Catalunya (UVic-UCC), Vic, Catalonia, Spain / ⁵ Faculty of Psychology and Education Sciences, Universitat Oberta de Catalunya (UOC), Barcelona, Catalonia, Spain

Table 1. Main characteristics and findings of works meeting the study criteria (N=58).

Population Group	Nº Studies (%)	Design (%)	Sample Size Range (% >500 Participants)	Psychosocial Consequences	Risk Factors
Affected by COVID-19	1 (2%)	Cross-sectional: 1 (100%)	103 (0%)	- Stress symptoms (100%)	- COVID-19 frontline worker (100%) - Lack of protective measures (100%)
Healthcare workers	24 (41%)	Cross-sectional: 24 (100%)	37; 7,143 (22%)	- Depressive symptoms (41%) - Anxiety (67%) - Stress symptoms (33%) - Insomnia (29%) - Perceived loneliness (4%) - PTSD (8%)	- Women (25%) - Nurses (12%) - Infected/suspected relatives (12%) - Living in rural areas (12%) - COVID-19 frontline worker (50%)
General population	35 (60%)	Cross-sectional: 33 (94%) Prospective: 2 (6%)	170; 52,730 (45%)	- Depressive symptoms (46%) - Anxiety (60%) - Stress symptoms (17%) - Insomnia (17%) - Perceived loneliness (3%) - PTSD (3%)	- Women (28%) - Young people (26%) - Low education level (11%) - Worried about infection (9%) - COVID-19 frontline worker (11%)

- Percentage in "Nº Studies" is according to total studies. Two reports investigated healthcare workers and the general population in the same study.
- Percentage in the rest of columns is according to the studies in each population group.
- "Sample Size Range" is referred to minimum and maximum values, except for affected by COVID-19, which is total sample size.
- General population included several subpopulations: Children/adolescents: 2 (4%); Young adults: 2 (4%); Pregnant/postpartum: 2 (4%); Older people: 1 (2%); Psychiatric disorders: 1 (2%); Epilepsy: 1 (2%).
- Abbreviations: PTSD, Post-Traumatic Stress Disorder.

Figure 2. Trends in published reports investigating psychosocial impact associated with COVID-19.



- Data are shown for 3 timepoints. Timepoints are based on the most recent search date of the accepted results in this conference (12th May). A previous exploratory date was considered 7 weeks before (24th March) and mostly up-to-date results 7 weeks later (2nd July).
- Original articles data are excluding the full-text review step.



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3. Relevant Practical Considerations



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1. HIV + General Population: Sharing Efforts



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1. HIV + General Population:
Sharing Efforts
2. **Validity, Feasibility, and Accuracy of
Neuropsychological Testing**

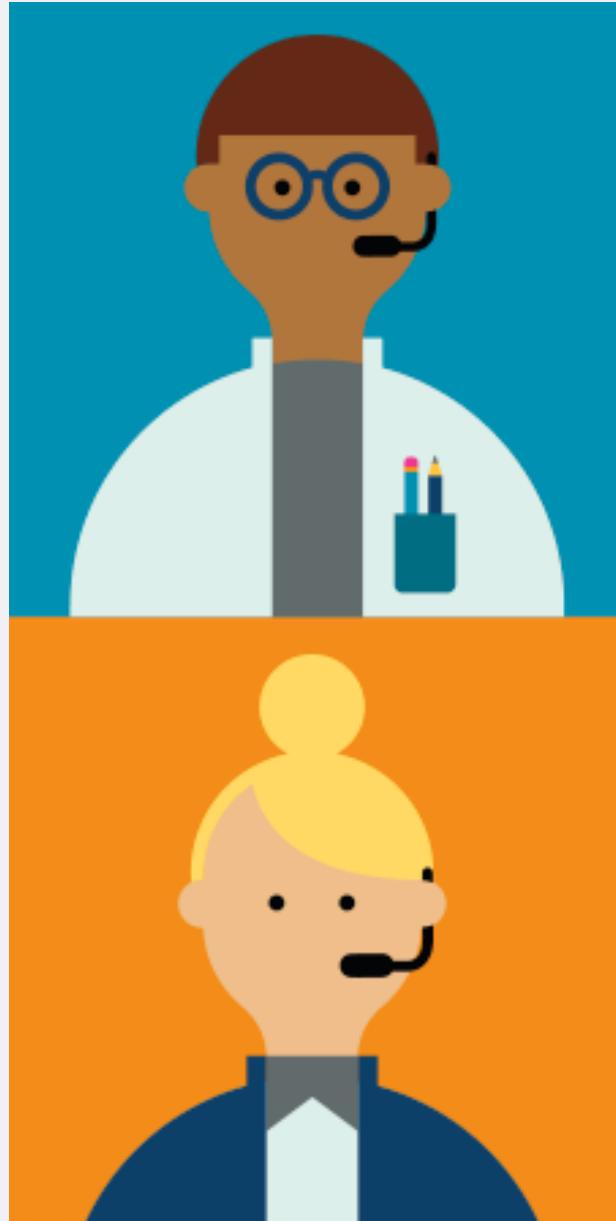


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1. HIV + General Population:
Sharing Efforts
2. Validity, Feasibility, and Accuracy of
Neuropsychological Testing
3. **Telehealth as an Emerging and
Promising Field**



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4. **Unique Opportunity for Health-
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4. Unique Opportunity for Health-
Related Outcomes Assessment
5. **Massive Research Ongoing, but
Still More Needed**



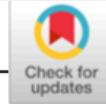
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LETTER TO THE EDITOR

International Journal of
Geriatric Psychiatry **WILEY**

Experience and results with a telehealth treatment program in patients with cognitive disorders during the COVID-19 pandemic



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