

NEUROPSYCHIATRY AND BEHAVIORAL NEUROLOGY

Olfactory dysfunction but not COVID-19 severity predicts severity of cognitive sequelae following SARS-CoV-2 infection in Amerindian older adults

Gabriela Gonzalez-Aleman¹ | Hernan P. Zamponi² | Leonardo Juarez-Aguaysol³ | Gabriela Kukoc⁴ | Maria Eugenia Dominguez⁴ | Belén Pini⁴ | Eduardo G Padilla⁵ | Maria Calvó⁵ | Silvia Beatriz Molina-Rangeon⁵ | Gonzalo Guerrero⁵ | Mariana Figueredo-Aguiar⁵ | Emiliano Fumagalli⁶ | Fabiana Vaca⁷ | Agustín Yécora⁷ | Traolach S Brugha⁸ | Sudha Seshadri⁹ | Heather M. Snyder¹⁰ | Gabriel A. de Erausquin^{11,12} | Alzheimer's Association Consortium on Chronic Neuropsychiatric Sequelae of SARS-CoV-2

¹Pontificia Universidad Catolica Argentina, Buenos Aires, Argentina

²Ministerio de Salud de Jujuy, Jujuy, Argentina

³Ministerio de Salud, San Salvador de Jujuy, Argentina

⁴Ministerio de Salud, San Salvador de Jujuy, Argentina

⁵FUNDACION FULTRA, San Salvador de Jujuy, Argentina

⁶Universidad Nacional de Jujuy, San Salvador de Jujuy, Argentina

⁷Ministerio de Salud de la Provincia de Jujuy, San Salvador de Jujuy, Argentina

⁸University of Leicester, Leicester, United Kingdom

⁹Glenn Biggs Institute for Alzheimer's & Neurodegenerative Diseases, University of Texas Health Science Center, San Antonio, TX, USA

¹⁰Alzheimer's Association, Chicago, IL, USA

¹¹South Texas Alzheimer's Disease Research Center, San Antonio, TX, USA

Abstract

Background: COVID-19 has affected more than 380 million people. Infections may result in long term sequelae, including neuropsychiatric symptoms. In older adults COVID-19 sequelae resemble early Alzheimer's disease, and may share risk factors and blood biomarkers with it. The Alzheimer's Association Consortium on Chronic Neuropsychiatric Sequelae of SARS-CoV-2 infection (CNS SC2) established harmonized definitions, ascertainment and assessment methodologies to evaluate and longitudinally follow up cohorts of older adults with exposure to COVID-19. We present one year data in a prospective cohort from Argentina.

Method: Participants (n = 766) are older adults (≥60 years) recruited from the provincial health registry containing all SARS-CoV-2 testing data. We randomly invite older adults stratified by PCR COVID-19 testing status regardless of symptom severity, between 3 and 6 months after recovery. Assessment includes interview with the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) and Clinical Dementia Rating scale (CDR); neurocognitive assessment; emotional reactivity scale; and neurological assessment including semiquantitative olfactory function test, motor function, coordination and gait.

Result: We assessed 88.4% infected participants and 11.6 % controls. Education is 10.36 ± 5.6 years and age is 66.9 ± 6.14 years. Level of care during

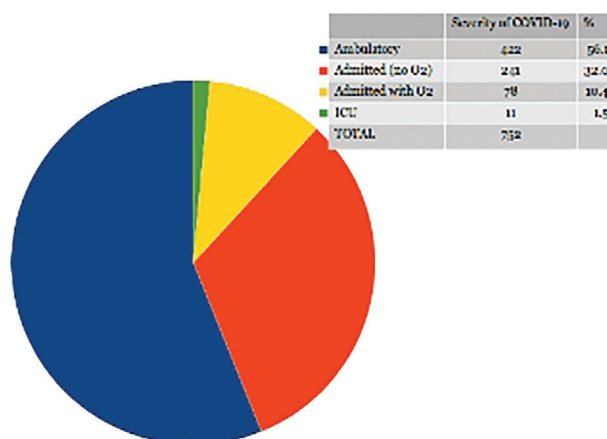
¹²Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases, San Antonio, TX, USA

Correspondence

Gabriela Gonzalez-Aleman, Pontificia Universidad Catolica Argentina, Buenos Aires, Argentina.
Email: gabigoa@gmail.com

COVID-19 is described in Figure 1. Normalized cognitive Z-scores categorize the cohort in 3 groups with decreased performance compared to normal cognition: memory only impairment (Single-domain, 11.7%); impairment in attention+executive function without memory impairment (Two-domain, 8.3%); and multiple domain impairment (Multiple domain, 11.6%). Logistic regression showed that severity of anosmia, but not clinical status, significantly predicts cognitive impairment. No controls had olfactory dysfunction. Cognitive impairment is defined as Z-scores below (-2) (Table 1). Clinical assessment with SCAN revealed functional memory impairment in two thirds of infected patients ($CDR \geq 1$), which was severe in half of them. Phone-based follow up at 1 year revealed high adherence (4 participants declined). Five were deceased at follow up. Rates of re-infection (between 10 and 23%) were not affected by the vaccination schedule (Table 2).

Conclusion: The longitudinal cohort had very high adherence. Persistent cognitive and functional impairment after SARS-CoV-2 infection is predicted by persistent anosmia but not by the severity of the initial COVID-19 disease.



Task	Z-SCORES/COGNITIVE IMPAIRMENT			
	Normal (N = 522)	Single domain (N= 86)	Two domain (N = 66)	Multidomain (N= 89)
WORD LIST- LEARNING (WMS-III)	-0.92	-1.58	-1.49	-2.16
WORD LIST- SHORT TERM MEMORY	-0.77	2.09	1.09	-2.32
WORD LIST- LONG TERM MEMORY	-0.2	-1.26	-0.52	-1.59
WORD LIST- RECOGNITION	-0.61	-1.31	-1.19	-2.02
ORAL TRAILS- VERBAL	-0.42	-0.68	-1.62	-2.35
ORAL TRAILS- VISUAL	-0.44	-0.72	-1.74	-2.02
ORAL TRAILS- MENTAL	-0.57	-0.96	-2.25	-2.61
ORAL TRAILS- VISUAL-MENTAL	-0.69	1.17	2.57	-2.9
ORAL TRAILS- SWITCHING	-0.58	-1.04	-2.16	2.67
5 DIGIT TEST- INHIBITION	-0.11	-0.05	-0.57	-0.5
5 DIGIT TEST- FLEXIBILITY	-0.35	-0.48	-0.92	-1.14

Results of 1-year phone survey		
Vaccine doses (#)	% of cohort	% reinfected
0	1.5	12.5
1	1.9	10.0
2	24.9	23.3
3	71.8	12.5