Impact of severity during COVID-19 infection on cognitive and global brain changes in post-COVID condition

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Introduction: Post-COVID condition (PCC) is an important sequela of COVID-19, characterised by symptom persistence for >3 months. Sars-cov-2's infection has been related to a decrease in cognitive performance (1) and brain changes (2) in PCC. Even so, PCC differences between mild and severe COVID-19 patients are still poor investigated.

Objectives: The main aim of this work is to study differences in cognition and global neuroimaging parameters in PCC patients classified according to COVID-19 severity.

Methods: Thirty-five hospitalized during the infection and 42 non-hospitalized PCC individuals from the Nautilus Project (ClinicalTrials.gov IDs: NCT05307549 and NCT05307575) underwent T1-weighted magnetic resonance imaging (MRI) and neuropsychological assessment. Global volumetric measures (white matter hypointensities (WMH), total gray and white matter volume) and mean cortical thickness were estimated using the automated Freesurfer software (7.1v,http://surfer.nmr.harvard.edu). Statistical analyses were carried out using the statistical package SPSS-27 (2016; Armonk, NY:IBM Corp.). Between-groups analyses were controlled by total intracranial volume and COVID-MRI time interval, and partial correlations by age and education. Statistical significance was set at p-value <0.05.

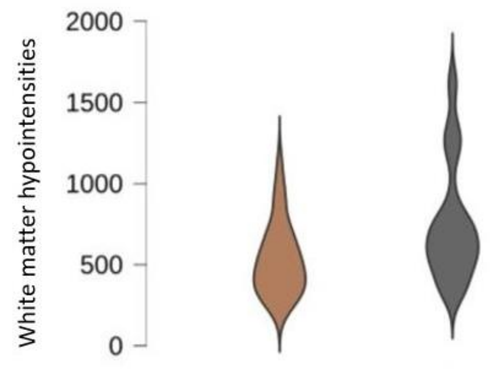
Results: Compared to non-hospitalized patients, hospitalized patients showed reduced performance in Rey Osterrieth Complex Figure test copy time (p=0.004) and immediate memory (p= 0.030), digit span forward (p=0.003), Digit Symbol test coding (p=0.043) and Trail Making test B (p=0.047) (Table 1), as well as increased WMH volume (p=0.008) (Table 2). No correlation was found between WMH and cognition.

	n	Mild (n= 42)	Severe (n=35)	Test stat/ p
MoCA	77	25.98 (2.36)	25.26 (2.99)	1.18/.243
RAVLT Total	77	43.98 (9.96)	42.06 (9.88)	0.85/.401
RAVLT delayed recall	76	8.79 (3.67)	8.21 (3.24)	0.72/.473
RAVLT recognition	76	11.98 (2.6)	11.41 (3.08)	0.87/.388
ROCF immediate memory accuracy	76	18.94 (5.57)	16.01 (5.97)	**2.21/.030**
ROCF delayed memory accuracy	77	19.39 (4.95)	17.37 (6.41)	1.56/.123
ROFC copy time	77	136.93 (54.61)	194.11 (99.72)	**-3.04/.004**
Digit span forward	77	6.05 (1.25)	5.17 (1.25)	**3.07/.003**
Digit span backwards	77	4.52 (1.09)	4.17 (1.10)	1.41/.263
DSC coding	77	66.50 (15.71)	58.26 (19.48)	**2.06/.043**
TMTA	77	37.79 (26.00)	45.94 (32.83)	-1.22/.228
TMTB	77	78.57 (43.87)	110.77 (84.64)	**-2.03/.047**
Stroop W	76	93.48 (25.74)	95.65 (17.10)	-0.42/.674
Stroop C	76	66.02 (15.86)	64.24 (13.23)	0.53/.601
Stroop WC	76	39.60 (8.93)	37.56 (11.70)	0.86/.392
PMR Total	77	43.24 (12.02)	39.74 (13.16)	1.27/.227
Animals	77	20.57 (5.45)	19.57 (5.91)	0.77/.443
BNT	77	53.26 (4.62)	51.89 (6.34)	1.10/.275

[Table 1] Group comparison of neuropsychological performance mild covid patients VS severe covid patients. *Abbreviations: HC, healthy controls; UPSIT, University of Pennsylvania Smell Identification Test; MoCA, Montreal Cognitive Assessment; ROFC, Rey–Osterrieth Complex Figure Test; RAVLT, Rey's Auditory Verbal Learning Test; RAVLT recall, total recall after 20 min; RAVLT recognition, total recognition after 20 min; RAVLT total, sum of correct responses from trial I to trial V; DSC, Digit Symbol Coding; Stroop W, Stroop Word; Stroop C, Stroop Color; Stroop WC, Stroop Word-Color; TMTA, Trail Making Test part A; TMTB, Trail Making Test part B; PMR: phonetic fluency; BNT, Boston Naming Test. Group differences between HC and COVID patients were tested using T-test. Measures are presented as mean (standard deviation).*

	Mild (n=41)	Severe (n = 35)	Test stat/p
WM-hypointensities	607.99 (241.07)	898.87 (514.60)	**7.35/.008**
GM total volume (cm3)	587274609.78 (132136936.06)	537813172.58 (210121204.47)	0.99/.324
WM total volume (cm3)	438.67 (58.87)	460.03 (65.57)	1.60/.210
Lh cortical thickness	2.49 (0.07)	2.47 (0.06)	1.82/.182
Rh cortical thickness	2.47 (0.07)	2.45 (0.06)	1.62/.208
Global mean CTh	2.48 (0.07)	2.46 (0.06)	1.76/.189

[Table 2] Group differences in global brain measures in mild and severe groups. Abbreviations: WM, white matter; GM, grey matter; lh, left hemisphere; rh, right hemisphere; CTh, cortical thickness. Group differences between mild and severe groups were tested using general linear model with interval of time between COVID onset and MRI as a covariate. Volume and WM-hypointensities were also covariate with TIV.



[Figure 1] White matter hypointensities distribution in PCC participants based on COVID-19 infection severity.

Conclusions: PCC participants who suffered severe COVID-19 infection showed worse cognitive performance involving working memory, visual memory and visuomotor speed. Moreover, it has increased WM abnormalities.

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