Post Covid Cognitive Impairment Neuroimaging Abnormalities on MRI- A Potential Biomarker

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BACKGROUND

Cognitive impairment (CI) is a feature of "long COVID" also known as Post-acute sequelae of SARS-COV-2 infection (PASC). Neuroinflammation has been causally implicated but as yet there are no definitive imaging biomarkers.

METHODS

This prospective longitudinal study enrolled 14 patients (Mean age 45, 10 females) with PASC CI (who had acute mild and non-hospitalised COVID infection) and 10 sex and age matched healthy controls. 13 had a follow up multi-modal MRI at 9-12 months (mean 10 months). All participants underwent DCE perfusion (an index of BBB integrity with Ktrans as the measurement), Diffusion Tensor Imaging (DTI) and single voxel MR spectroscopy (MRS) of the frontal cortex/white matter and the brainstem in addition to brain anatomical MRI. Between group analyses were used to determine which MRI outcomes were significantly different in patients with PASC CI relative to controls.

Post acute mild to moderate COVID-19 cognitive impairment is associated with an impaired blood brain barrier, frontal and brainstem inflammation and disturbed white matter tracts all of which variably improve after 10months.

RESULTS - Baseline

DCE Perfusion: significantly increased Ktrans (i.e., BBB impairment) across all regions, but more specifically in the frontal white matter and brain stem (p=< 0.005),

Diffusion Tensor Imaging (DTI): Reduction in white matter integrity (increased diffusivity - greater radial and mean diffusivity). **Correlation:** Increased Ktrans was correlated with increased both radial and mean diffusivity (r=0.9) in all tested brain regions.

MR Spectroscopy (MRS): Reduction in NAA (i.e., neuronal injury) and mild reduction of Glx (i.e., excitotoxicity) in the frontal white matter and brain stem (p=0.004),

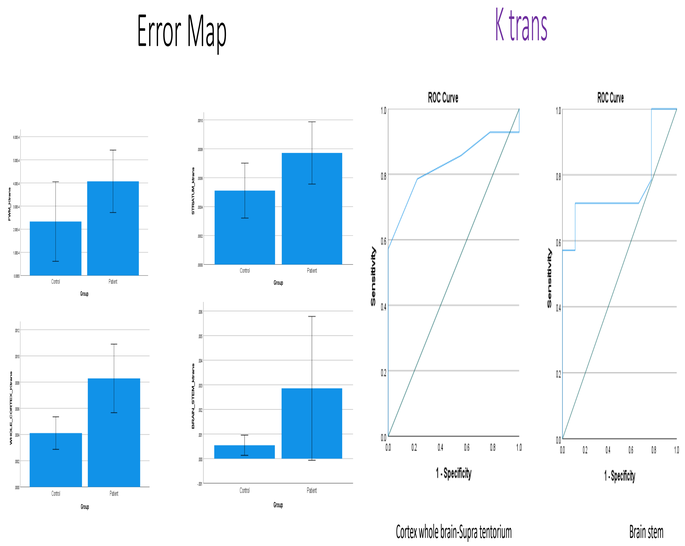
RESULTS - Follow up

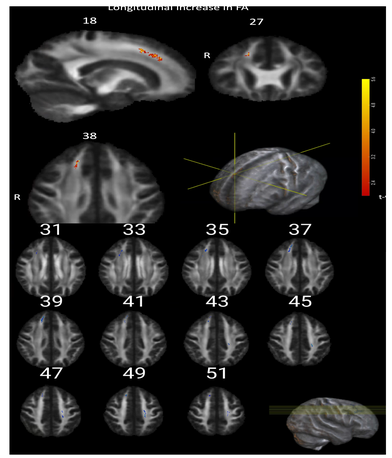
DCE Perfusion: Ktrans significantly improved at the follow up (p= 002596 Z=-2.794872) with no difference between subjects and controls indicating BBB normalisation (p= 0.442418, z= -0.144841).

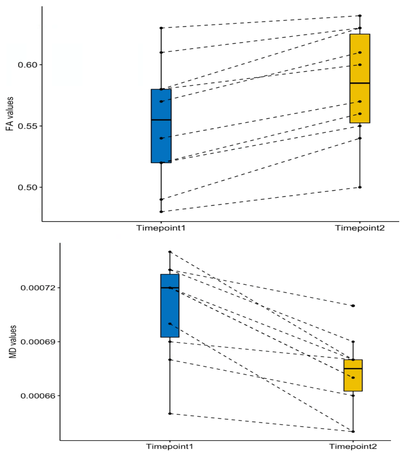
DTI: White matter integrity also improved especially in the fractional anisotropy values in the executive networks (p=< 0.00045).

MRS showed significant improvement in the NAA in the frontal white matter, but Glx remain high compared to the controls (p=0.0006).

Differences in K trans between controls and patients







At follow-up TBSS shows increased connectivity in the executive networks and reduced mean diffusivity in the white matter across the whole brain

Multi-parametric probability values at two study time points		
	Baseline	Follow-up
Ktrans (Mean)	0.001	0.0005
MRS NAA (Frontal White Matter)	0.06	0.08
MRS NAA (Brain Stem)	0.002	0.14
MRS MYO (Frontal White Matter)	0.004	0.15
MRS GLX (Frontal White Matter)	0.0001	0.004
MRS GLX (Brain Stem)	0.0006	0.0006

CONCLUSIONS

PASC CI was characterised by reversible diffuse BBB impairment, neuronal/axonal injury likely initiated by excitotoxicity. BBB impairment was associated with reversible white matter injury. These are suggestive biomarkers for the presence, severity and prognosis of PASC CI. Such biomarkers could underpin appropriate trial design and timing of intervention.

ADDITIONAL KEY INFORMATION

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