

BACKGROUND

Long COVID is a recognised condition following COVID-19 infection, affecting approximately 10–15%, even occurring after a mild initial illness. It causes multisystem involvement, including the brain, resulting in cognitive and psychiatric changes.

Impairments are particularly pronounced in ‘higher order’ cognitive domains, such as executive function, sustained attention, verbal learning and memory.

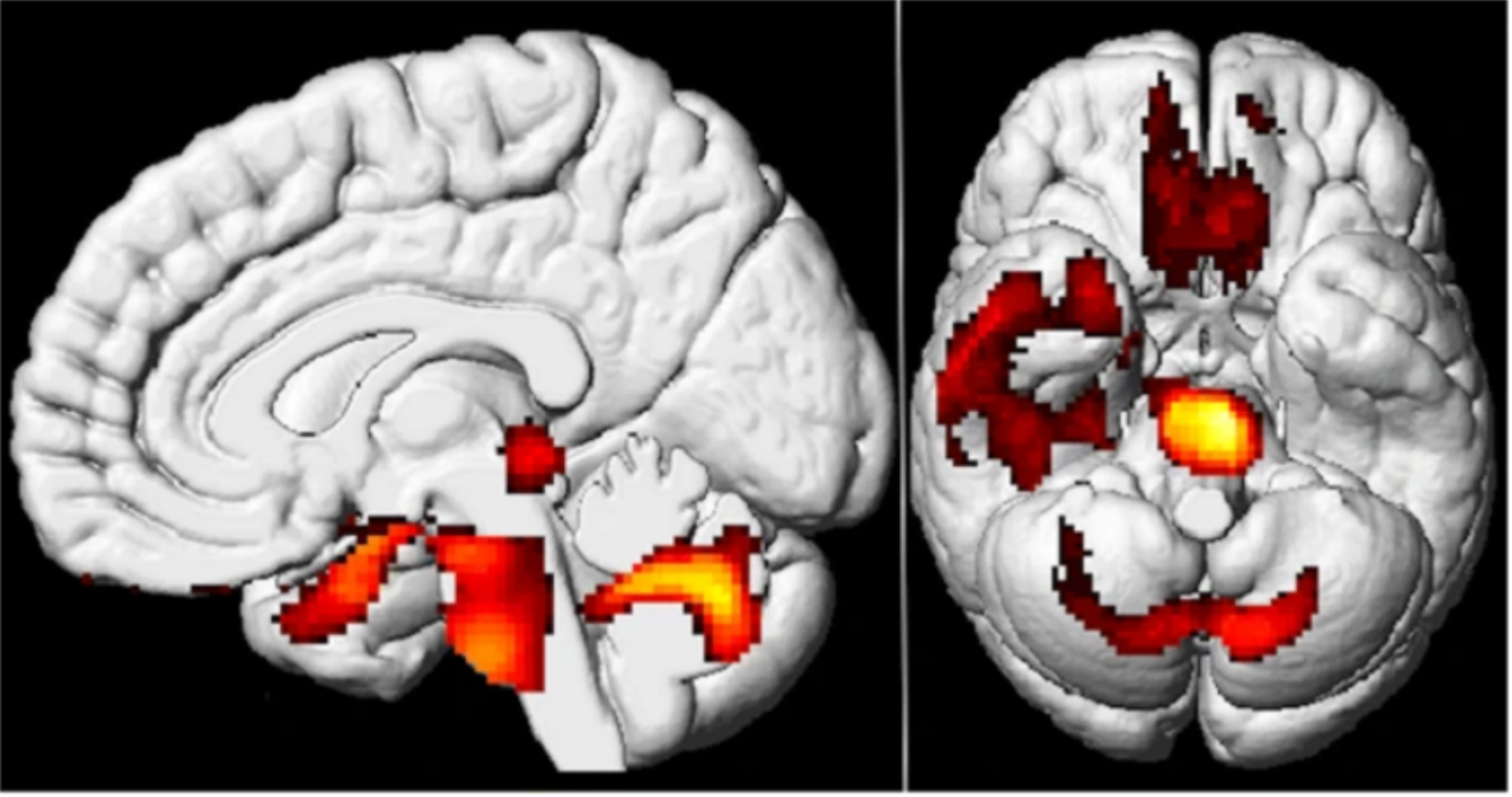
Neuroimaging using FDG PET/CT scanning shows FDG hypometabolism in a consistent pattern of bilateral hypometabolism in rectal/orbital gyrus, olfactory gyrus; right temporal lobe, amygdala and hippocampus, extending to the right thalamus, pons/medulla brainstem, and cerebellum [Figure 1] [1].

These metabolic clusters show high discrimination between patients and healthy subjects.

Studies report abnormal scores on cognitive testing, and the characteristic Long-COVID PET/CT pattern, but few have looked at correlations between the absolute cognitive test score and the imaging changes. Even fewer have looked at patient reported symptoms in relation to the cognitive tests and imaging changes.

In this study we evaluate whether PET/CT difference in regional cerebral glucose metabolism correlate with subjective cognitive symptoms, and/or poorer cognitive performance.

Fig.1



Brain ¹⁸F-FDG PET hypometabolism in patients with long COVID. In comparison to healthy subjects, the patients exhibit hypometabolism in the bilateral rectal/orbital gyrus, including the olfactory gyrus; the right temporal lobe, including the amygdala and the hippocampus, extending to the right thalamus; the bilateral pons/medulla brainstem; the bilateral cerebellum (p-voxel < 0.001 uncorrected, p-cluster < 0.05 FWE-corrected; SPM8 3D rendering)

Methods

- Participants in a Long COVID study with subjective brain fog were evaluated cognitively with a symptom questionnaire (MSQ), Montreal Cognitive Test (MoCA) [2], and computer-based Cognigram® [3].

- All underwent a baseline FDG PET/CT scan within 6-months of their cognitive testing

- A standard 18F-FDG PET/CT brain protocol was utilized. This included patient fasting for at least 6 hours prior to 18F-FDG radiotracer injection and a serum glucose reading below 8.9 mmol/L before injection

- Total subjective cognitive score (MSQ), MoCA, and composite domains of Cognigram® (psychomotor/attention; learning/working memory) were compared to the FDG PET/CT results.

- The latter were grouped as normal versus abnormal (mild, moderate, severe, inconclusive) compared to age and sex matched standards.

- Radiologic evaluation was undertaken blinded to clinical and cognitive test results.

Results

88 participants completed all tasks.

Subjective cognitive score (MSQ) (Figure 2): grouped by both total severity and number of complaints

Average MoCA: 27/30 (18-30)

Cognigram®: Learning/working memory 99.7 (60-128); psychomotor/attention 79.7 (-21.4 – 114)

FDG PET/CT (Figure 3):

27% within normal

49% mild hypometabolism

20% moderate hypometabolism

0% severe hypometabolism

3% inconclusive

Using Spearman correlations (Table 1): MoCA and Cognigram® were correlated (0.26; p 0.012). Only Cognigram® scores were highly correlated with subjective cognitive complaints (-0.381; p<.001).

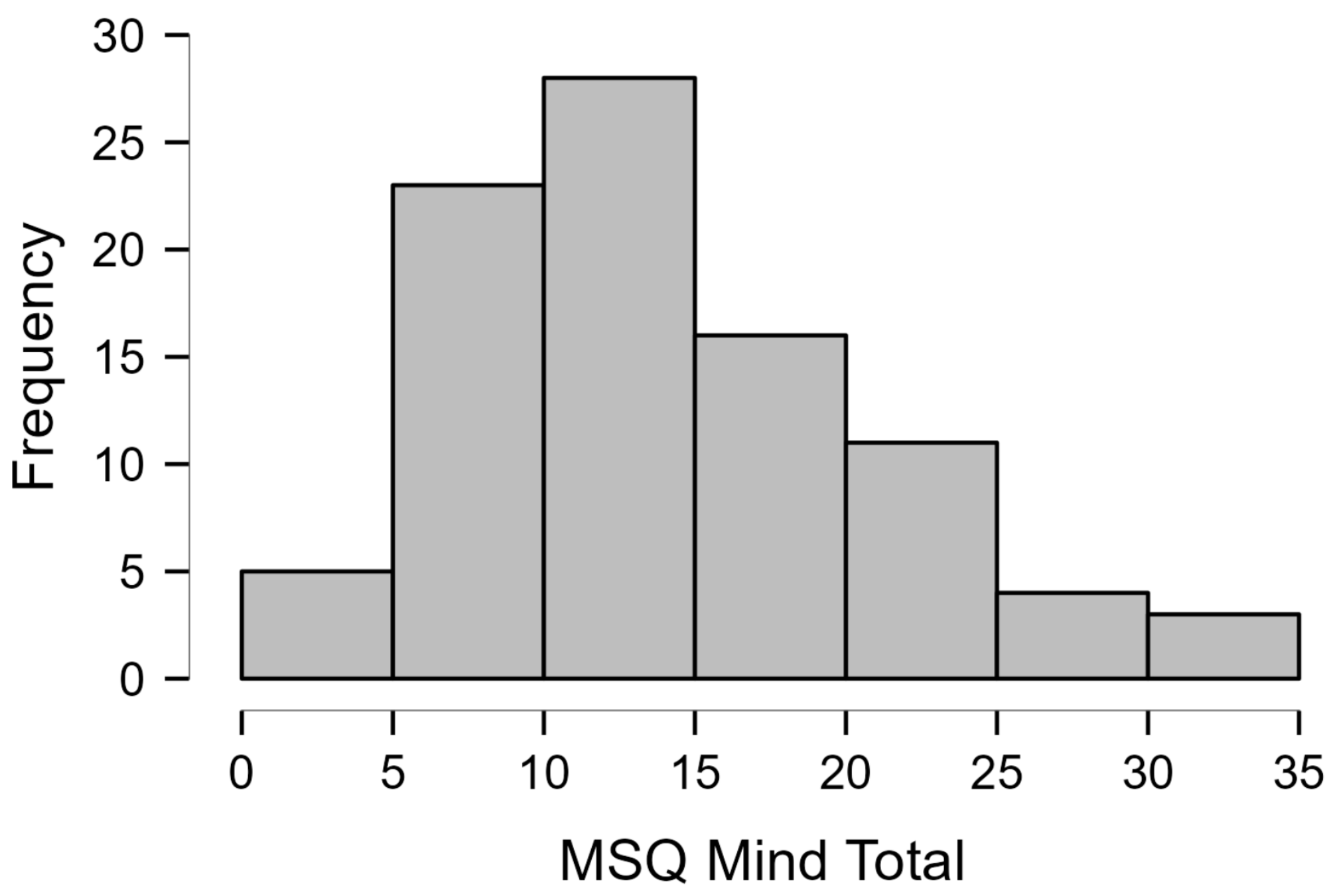
The PET/CT results were not correlated with any cognitive scores.

Cognigram Correlations

Table 1: Spearman Correlations with PET/CT changes, cognitive scores, and subjective cognitive complaints.

Spearman's Correlations ▼				
		n	Spearman's rho	p
cog_psychoaftcomp	- cog_learnmemcomp	93	0.082	0.437
cog_psychoaftcomp	- moca_total	93	0.260*	0.012
cog_psychoaftcomp	- pet_result_specific	87	0.067	0.540
cog_psychoaftcomp	- pet_result_1	87	0.050	0.649
cog_psychoaftcomp	- cog_learn	93	0.170	0.104
cog_psychoaftcomp	- cog_mem	93	0.068	0.517
cog_psychoaftcomp	- cog_psych	93	0.944***	< .001
cog_psychoaftcomp	- cog_att	93	0.963***	< .001
cog_psychoaftcomp	- msq_poor_memory	90	~0.281**	0.007
cog_psychoaftcomp	- msq_confusion	90	~0.388***	< .001
cog_psychoaftcomp	- msq_poor_concentration	90	~0.384***	< .001
cog_psychoaftcomp	- msq_poor_physical_coordination	90	~0.264*	0.012
cog_psychoaftcomp	- msq_poor_decision_making	90	~0.324**	0.002
cog_psychoaftcomp	- msq_stuttering	90	~0.122	0.251
cog_psychoaftcomp	- msq_slurred_speech	90	~0.098	0.359
cog_psychoaftcomp	- msq_learning_disabilities	90	~0.175	0.100
cog_psychoaftcomp	- mind_total	90	~0.381***	< .001
cog_learnmemcomp	- moca_total	93	0.220*	0.034
cog_learnmemcomp	- pet_result_specific	87	~0.052	0.633
cog_learnmemcomp	- pet_result_1	87	~0.075	0.488
cog_learnmemcomp	- cog_learn	93	0.796***	< .001
cog_learnmemcomp	- cog_mem	93	0.863***	< .001
cog_learnmemcomp	- cog_psych	93	0.063	0.546
cog_learnmemcomp	- cog_att	93	0.117	0.265
cog_learnmemcomp	- msq_poor_memory	90	~0.209*	0.048
cog_learnmemcomp	- msq_confusion	90	~0.227*	0.032
cog_learnmemcomp	- msq_poor_concentration	90	~0.105	0.323
cog_learnmemcomp	- msq_poor_physical_coordination	90	~0.259*	0.014
cog_learnmemcomp	- msq_poor_decision_making	90	~0.107	0.316
cog_learnmemcomp	- msq_stuttering	90	~0.032	0.766
cog_learnmemcomp	- msq_slurred_speech	90	~0.140	0.189
cog_learnmemcomp	- msq_learning_disabilities	90	~0.068	0.526
cog_learnmemcomp	- mind_total	90	~0.181	0.087

Figure 2: Graph showing frequency of subjective cognitive complaints.



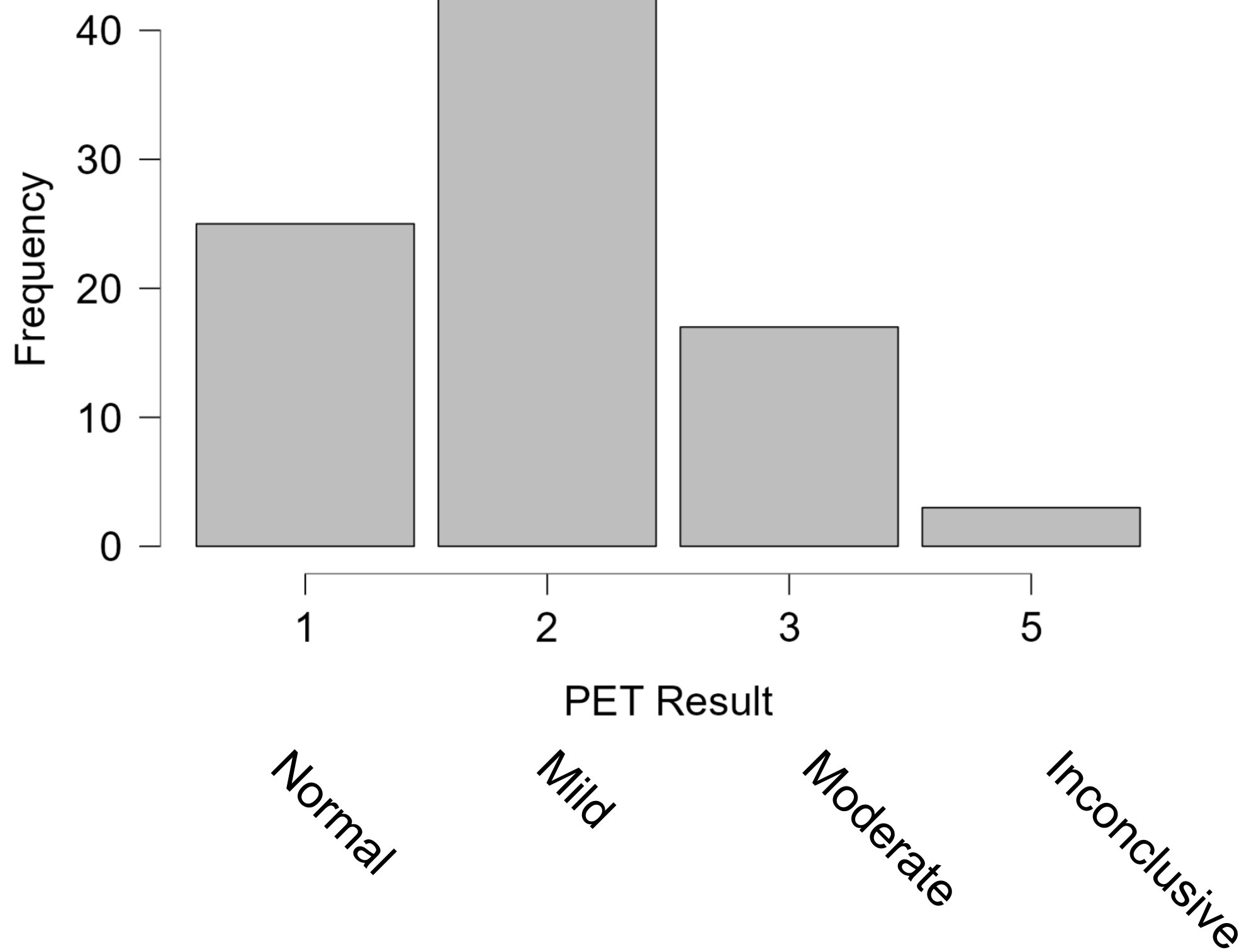
POINT SCALE
0 = Never or almost never have the symptom
1 = Occasionally have it, effect is not severe
2 = Occasionally have, effect is severe
3 = Frequently have it, effect is not severe
4 = Frequently have it, effect is severe

MIND

- Poor memory
- Confusion, poor comprehension
- Poor concentration
- Poor physical coordination
- Difficulty in making decisions
- Stuttering or stammering
- Slurred speech
- Learning disabilities

Total 0

Figure 3: Graph showing frequency of PET/CT versus normal.



Conclusions

- This study shows high correlation between reported cognitive complaints, and objective cognitive testing with the Cognigram® but not the MoCA.
- There was no apparent correlation with global PET/CT abnormalities.
- Analysis on specific domains of PET/CT abnormalities may show a correlation not identified in this analysis.

Acknowledgements

We would like to acknowledge the contributions of all participants, who gave up time and their limited energy capacity to participate in this study. We would like to also thank the University Hospital Foundation for funding the research, and the research study team members.

References

- Guedj E, et al. 18F-FDG brain PET hypometabolism in patients with long COVID. European Journal of Nuclear Medicine and Molecular imaging. 2021 Aug;48(9):2823-33
- Nasreddine, Ziad S., et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. Journal of the American Geriatrics Society 2005 53(4): 695-699.
- Cognigram Clinician User Manual V7.0