

# BBB permeability measurement could be a sensitive biomarker of cognitive impairment in mild TBI

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## Introduction

- The blood-brain barrier (BBB) disruption has been suggested as a contributor to traumatic brain injury (TBI).
- However, the temporal relationship between BBB disruption and post-traumatic cognitive dysfunction is not elucidated yet.
- We aimed to evaluate the temporal changes and relationship of BBB permeability and cognitive function, using dynamic contrast-enhanced (DCE) MRI and volumetry analysis in mild TBI.

## Methods

- This prospective longitudinal study included nineteen patients (mean age, 59 ± 12 years; 6 women) diagnosed with mild TBI (Glasgow Coma Scale >13) from March 2020 to March 2022.
- All patients underwent DCE T1-weighted imaging with a 3T scanner at three-time points; 1 week (W), 1 month (M), and 3M after the injury.
- The regional brain volumes were segmented using 3D T1-weighted sequences; BBB permeability (Ktrans) was determined using DCE MRI and the Patlak model approach.
- Mini-mental status exam (MMSE) was assessed for cognitive function measures.
- We used Spearman correlation analysis to evaluate the relationship of imaging biomarkers and cognition.

## Results

measurements (Ktrans) in the Gray matter (GM) cortex showed negative correlation with MMSE at 1W ( $p < 0.05$ ) (Table 2, Figure 1). Especially, Ktrans of GM showed significant correlation at 1W with a negative tendency at 1M and 3M. However, GM regional volume showed no significant correlation other than occipital in at 1W and 1M (Table 3).

## Conclusion

These data suggest that increased BBB permeability is correlated with cognitive dysfunction at the early stage after mild TBI. Additionally, BBB permeability biomarker could be a more sensitive biomarker than regional volume to reflect the cognitive impairment in mild TBI.

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**Table 1. Demographics of enrolled patients (N=19)**

Variables	Mean±SD or Median(Q1-Q3) or N(%)
Age, mean ± SD (years)	59.21±11.96
Sex, N (%)	
Male	13 (68.4)
Female	6(31.6)
Initial GCS	15(15-15)
Education year	12(9-16)
MMSE	
1 week	28(27-30)
1 month	30(28.75-30)
3 months	29(28-30)

SD, standard deviation; GCS, Glasgow Coma Scale; MMSE, Mini-mental status exam.

**Table 2. Correlation between Ktrans, regional volume and cognitive function tests**

	1W		1M		3M	
	Correlation Coefficient	Sig. (2-tailed)	Correlation Coefficient	Sig. (2-tailed)	Correlation Coefficient	Sig. (2-tailed)
GM Kcr*1000						
GM Lt cingulate	-.508*	0.037	-0.500	0.069	-0.233	0.423
GM Rt cingulate	-.505*	0.039	-0.436	0.119	0.005	0.987
GM Lt Frontal	-.487*	0.047	-0.409	0.146	0.095	0.746
GM Rt Frontal	-0.411	0.101	-0.372	0.190	0.021	0.943
GM Lt Temporal	-.573*	0.016	-0.284	0.325	0.158	0.589
GM Rt Temporal	-0.417	0.096	-0.372	0.190	0.019	0.950
GM Lt Insular	-.514*	0.035	-0.294	0.308	0.161	0.584
GM Rt Insular	-0.431	0.084	-0.348	0.223	-0.147	0.617
GM Lt Occipital	-.543*	0.024	-0.392	0.166	-0.137	0.640
GM Rt Occipital	-0.457	0.065	-0.500	0.069	0.077	0.794
GM Lt Parietal	-.577*	0.015	-0.328	0.252	0.030	0.918
GM Rt Parietal	-0.369	0.145	-0.274	0.342	-0.009	0.975

(\*p-value < 0.05)

**Table 3. Spearman correlation with MMSE and GM regional volume**

	1W		1M		3M	
	Correlation Coefficient	Sig. (2-tailed)	Correlation Coefficient	Sig. (2-tailed)	Correlation Coefficient	Sig. (2-tailed)
GM Lt cingulate	0.091	0.737	-0.023	0.937	0.405	0.151
GM Rt cingulate	0.011	0.969	-0.152	0.605	0.307	0.285
GM Lt frontal	0.193	0.474	0.049	0.868	0.002	0.994
GM Rt frontal	0.018	0.947	-0.023	0.937	0.216	0.457
GM Lt temporal	-0.243	0.364	0.023	0.937	-0.072	0.806
GM Rt temporal	-0.161	0.551	0.182	0.533	-0.295	0.305
GM Lt Insular	0.196	0.467	0.126	0.668	-0.191	0.514
GM Rt Insular	0.138	0.609	-0.126	0.668	0.077	0.794
GM Lt Occipital	0.511*	0.043	0.275	0.342	-0.012	0.969
GM Rt Occipital	0.382	0.145	0.575*	0.031	-0.035	0.906
GM Lt Parietal	0.224	0.405	0.077	0.793	0.119	0.686
GM Rt Parietal	0.310	0.242	0.421	0.134	-0.261	0.368

(\*p-value < 0.05)

**Figure 1. Correlation between Ktrans and MMSE at 1 week, 1 month, and 3 months**

