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Relationship between BBB permeability and cognitive dysfunction in mild traumatic brain injury

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Purpose

- 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) and Montreal Cognitive Assessment (MoCA) were assessed for cognitive function measures.
- We used Friedman test to show temporal changes, and linear mixed model analysis to evaluate the effect of BBB permeability and time on cognition after adjusting for age, sex, and education year. Univariable linear regression was conducted to evaluate the predictive value of BBB permeability and volume at 1W and 1M in cognitive function at 3M.

Results

- Median MoCA at 1W, 1M, and 3M were 26 (interquartile range, 24-28), 29 (26-30), and 28 (26.3-30), respectively (Table 1), and had significant changes as recovering in 1M and slight decline at 3M, with inverted U-shape over time (p=0.001). In contrast, MMSE and BBB permeability as well as regional volume in the brain did not differ over time.
- BBB permeabilities in the cortex [Gray matter (GM) 6 areas; frontal, temporal, parietal, occipital, cingulate, and insular cortex] and white matter (WM) were negatively correlated with MMSE score, regardless of time points (p<0.05) (Table 2, Figure 1). Especially, Ktrans of GM left cingulate and WM left insular showed significant correlation at 1W with a negative tendency at 1M and 3M.
- In a linear mixed model, lower left insular (p=0.041) and right parietal (p=0.042) cortex volume was the imaging predictor of lower MMSE, while the volume of left temporal cortex was a predictor of MoCA (p=0.028) after adjusting age, sex, and education year.
- Rt parietal volume at 1W (p=0.015) and age (p=0.025) were predictors of MoCA at 3M in univariable linear regression. However, BBB permeability of the entire areas in the GM and WM did not show prognostic value.

Table1. 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)
Intial 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)
MoCA-K	
1 week	26(24-28)
1 month	29(26-30)
3 months	28(26.25-30)

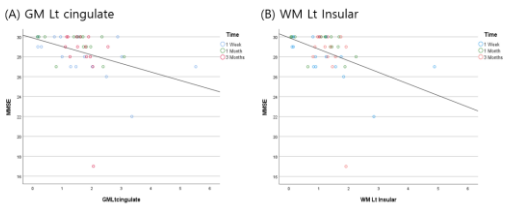
SD, standard deviation; GCS, Glasgow Coma Scale; MMSE, Mini-mental status exam; MoCA-K, Montreal Cognitive Assessment-Korean.

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

	Ktrans_GM		Ktrans_WM		Regional volume to ICV	
	MMSE	MoCA	MMSE	MoCA	MMSE	MoCA
Lt cingulate	**-0.448****	-0.165	**-0.402****	-0.138	0.151	0.198
Rt cingulate	**-0.373***	-0.088	**-0.368***	-0.100	0.079	-0.01
Lt frontal	**-0.348***	-0.13	**-0.370***	-0.148	0.103	0.104
Rt frontal	**-0.322***	-0.048	**-0.336***	-0.063	0.132	0.068
Lt temporal	**-0.390****	-0.156	**-0.339***	-0.081	-0.156	-0.105
Rt temporal	**-0.362***	-0.155	**-0.370***	-0.130	-0.032	0.022
Lt insular	**-0.364***	-0.131	**-0.423****	-0.153	0.116	-0.009
Rt insular	**-0.398****	-0.157	**-0.357***	-0.091	0.058	0.09
Lt occipital	**-0.402****	-0.1	**-0.378***	-0.122	0.185	0.144
Rt occipital	**-0.383****	-0.153	**-0.373***	-0.094	0.277	0.23
Lt parietal	**-0.385****	-0.136	**-0.406****	-0.129	0.076	0.093
Rt parietal	-0.293	0.053	**-0.317***	0.022	0.238	0.390**

***. p<0.01*
**. p<0.05*

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



Conclusion

These data suggest that increased BBB permeability is correlated with cognitive dysfunction at the early stage after mild TBI. Taken together with BBB permeability change, decreased volume of insular, parietal, and temporal cortex might be useful for the prediction of long-term cognitive impairment in mild TBI. Further studies with long-term follow-up are needed.

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