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Pharmacological inhibition of fatty acid-binding protein 4 is neuro-protective in the acute phase of ischemic stroke

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Introduction

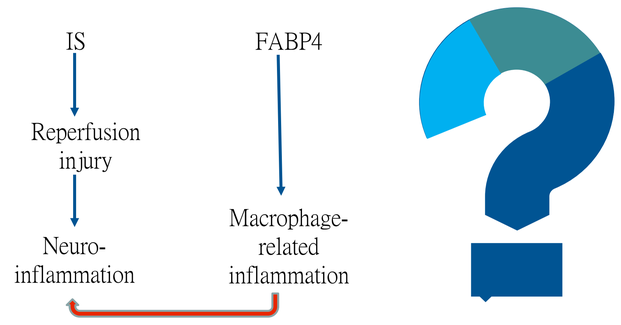
Ischemic stroke (IS)

1. IS is the second leading cause of death worldwide. MCAO is the most widely used rodent IS model.
2. Thrombolysis, the only FDA-approved treatment for IS, is incapable to cure ischemic-reperfusion (IR) injury.
3. The IR injury is especially attributed to neuro-inflammation in the acute phase of IS.

Fatty acid-binding protein 4 (FABP4)

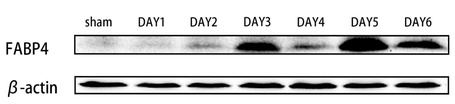
1. FABP4 coordinates lipid responses and macrophage-related inflammation.
2. Clinical data: the serum FABP4 elevation has a positive correlation with IS severity.
3. Experimental result: FABP4 exacerbates IS by disrupting the brain-blood barrier.

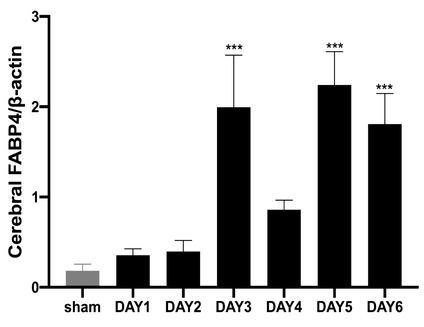
However, whether and how FABP4 inhibitor would protect IS remain obscure.



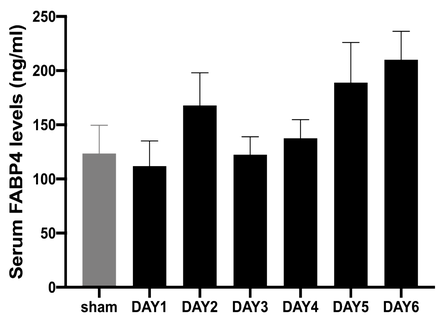
Results

1. FABP4 increased with two expression peaks after ischemic brain injury in MCAO mice.



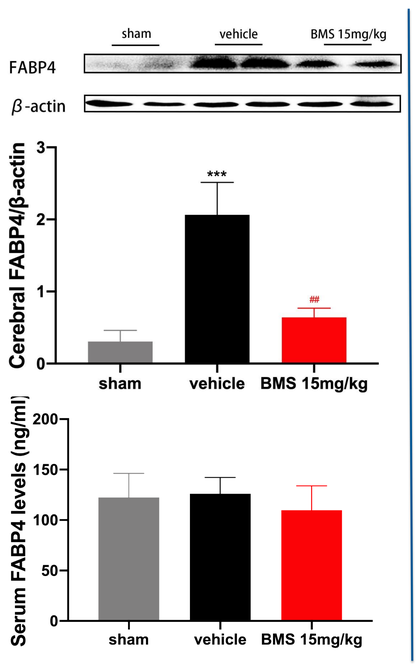


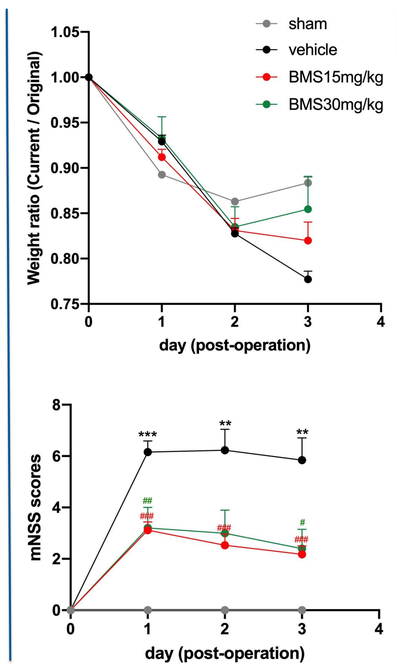
In the brain (ischemic hemisphere)

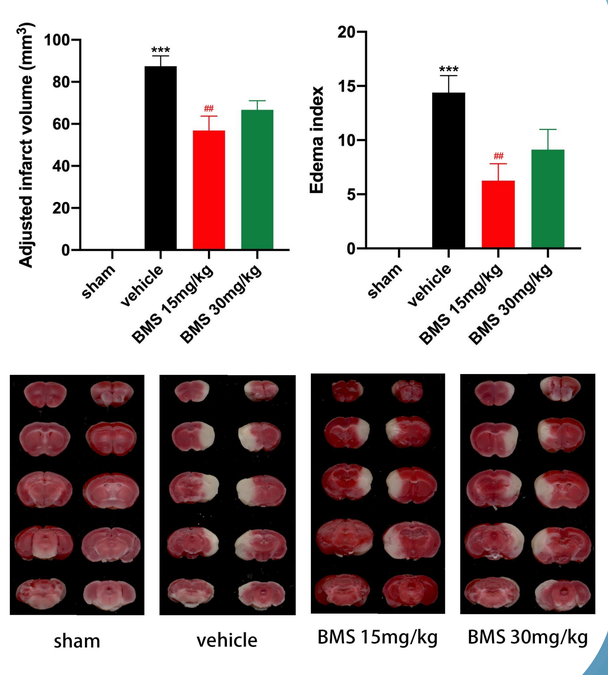


In peripheral blood

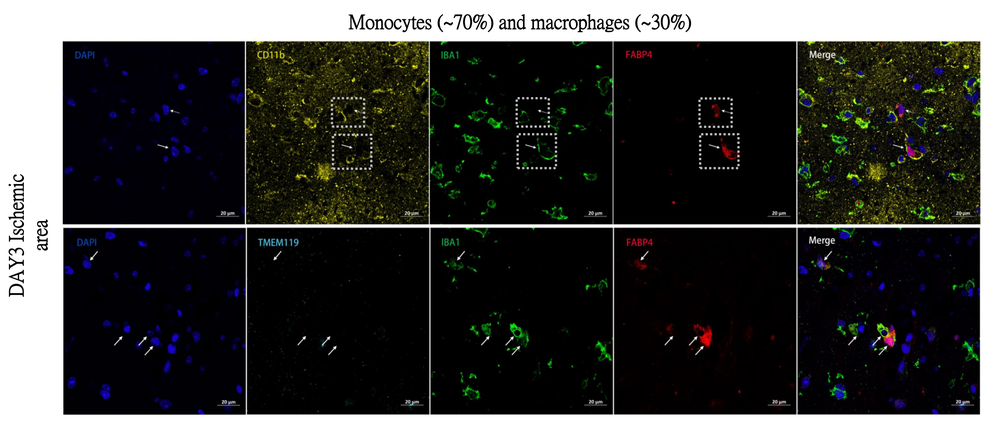
3. FABP4 inhibitor was neuro-protective in MCAO mice.

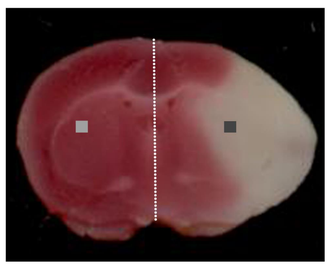






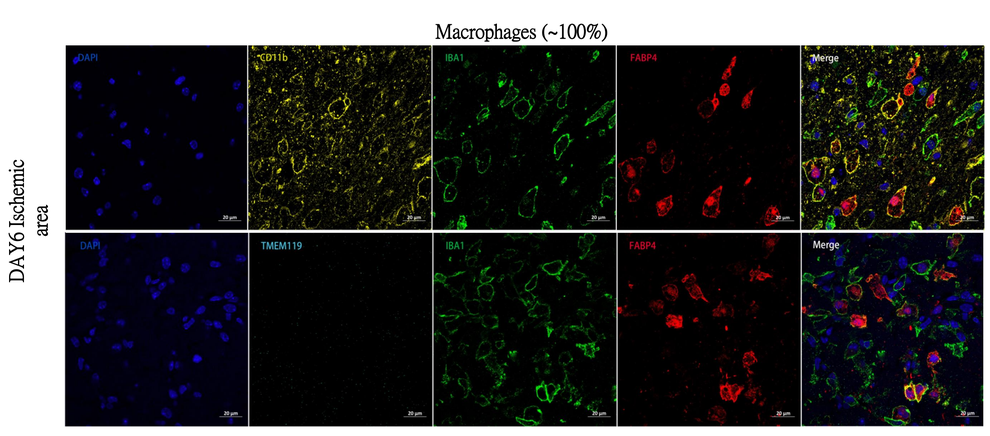
2. Cellular expression of cerebral FABP4: monocytes and macrophages.

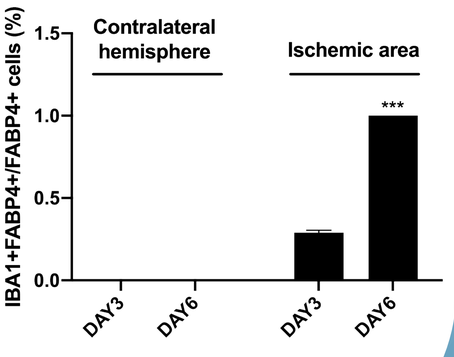




Contralateral hemisphere

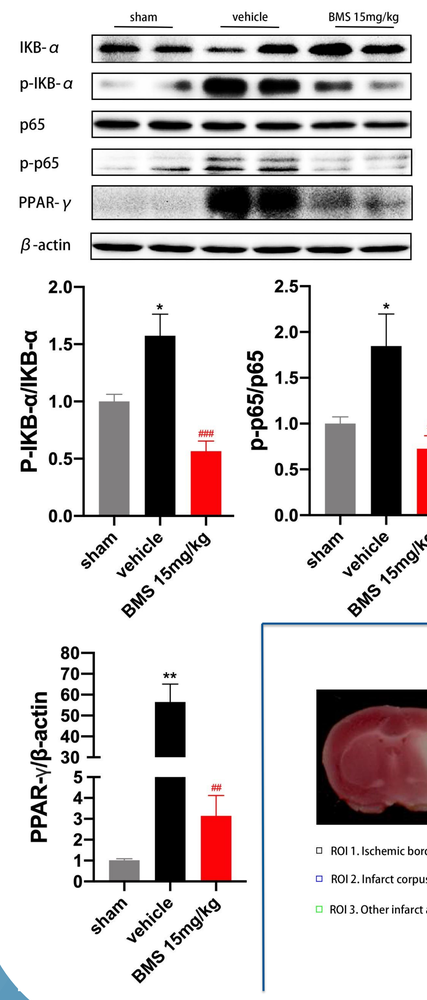
Ischemic area

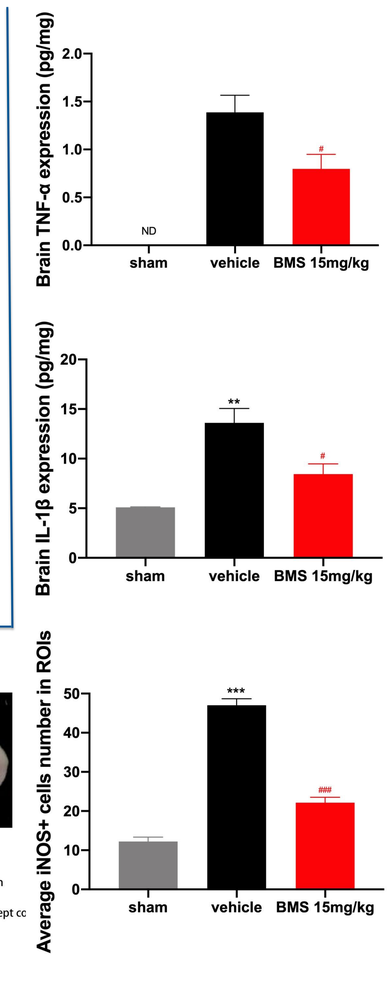




Monocyte: CD11b+ IBA1- TMEM119-
Macrophage: CD11b+ IBA1+ TMEM119-
Microglia: CD11b+ IBA1+ TMEM119+

4. FABP4 inhibitor decreased neuro-inflammation of MCAO mice in acute phase.





Conclusion

Pharmacological inhibition of FABP4 is neuro-protective in the acute phase of the mouse IS model. Its beneficial effects are achieved, at least in part, via regulating NF-kappa B and PPAR-gamma signalling pathways-mediated neuroinflammation.