

AppSAA mice have blood brain barrier dysfunction and reversible cognitive impairment at 8 months of age

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P3-05

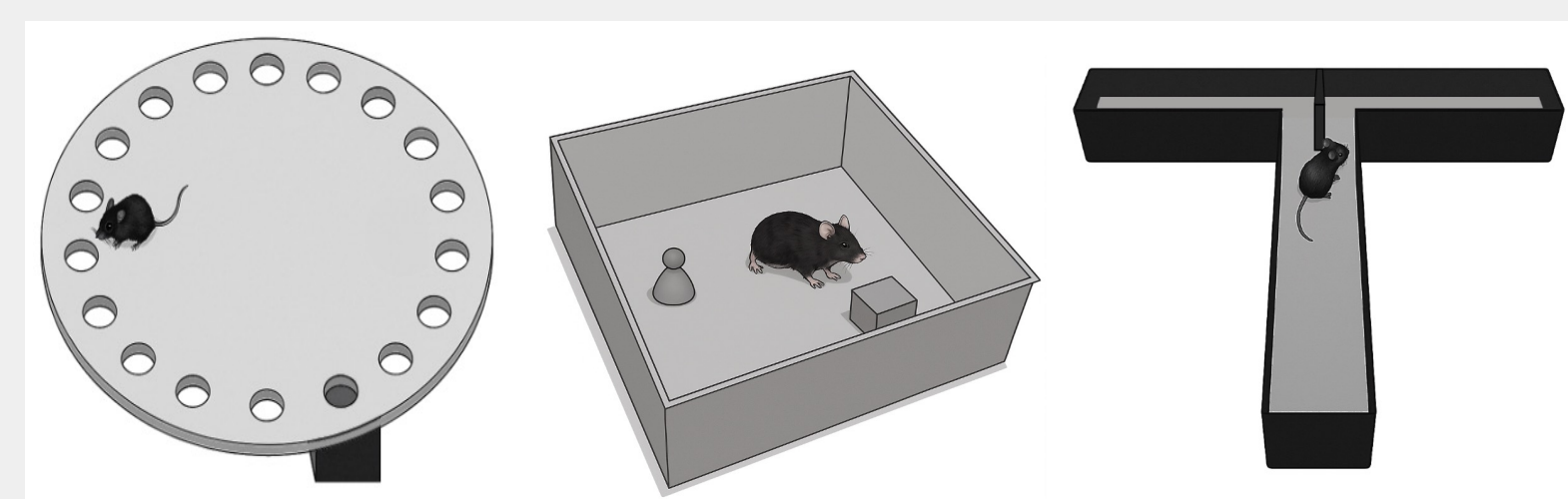
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Introduction

- Blood brain barrier dysfunction (BBBd) increases in aging and AD^{1,2}, but it remains unclear whether there is a direct link between BBBd and amyloid^{3,4}.
- AppSAA is a transgenic mouse model that accumulates amyloid plaques from 4 months onwards⁵.
- IPW is a TGF β inhibitor that has been shown to reverse BBBd associated neuroinflammation and cognitive impairment in aged wild-type mice¹.
- IPW has further been shown to reduce BBB leakage directly in aged wild-type mice (manuscript in preparation).
- Here, we investigate whether the presence of amyloid plaques accelerates BBBd in mice, and whether IPW treatment in AppSAA mice improves cognition.**

Methods

Behavior



Immunohistochemistry

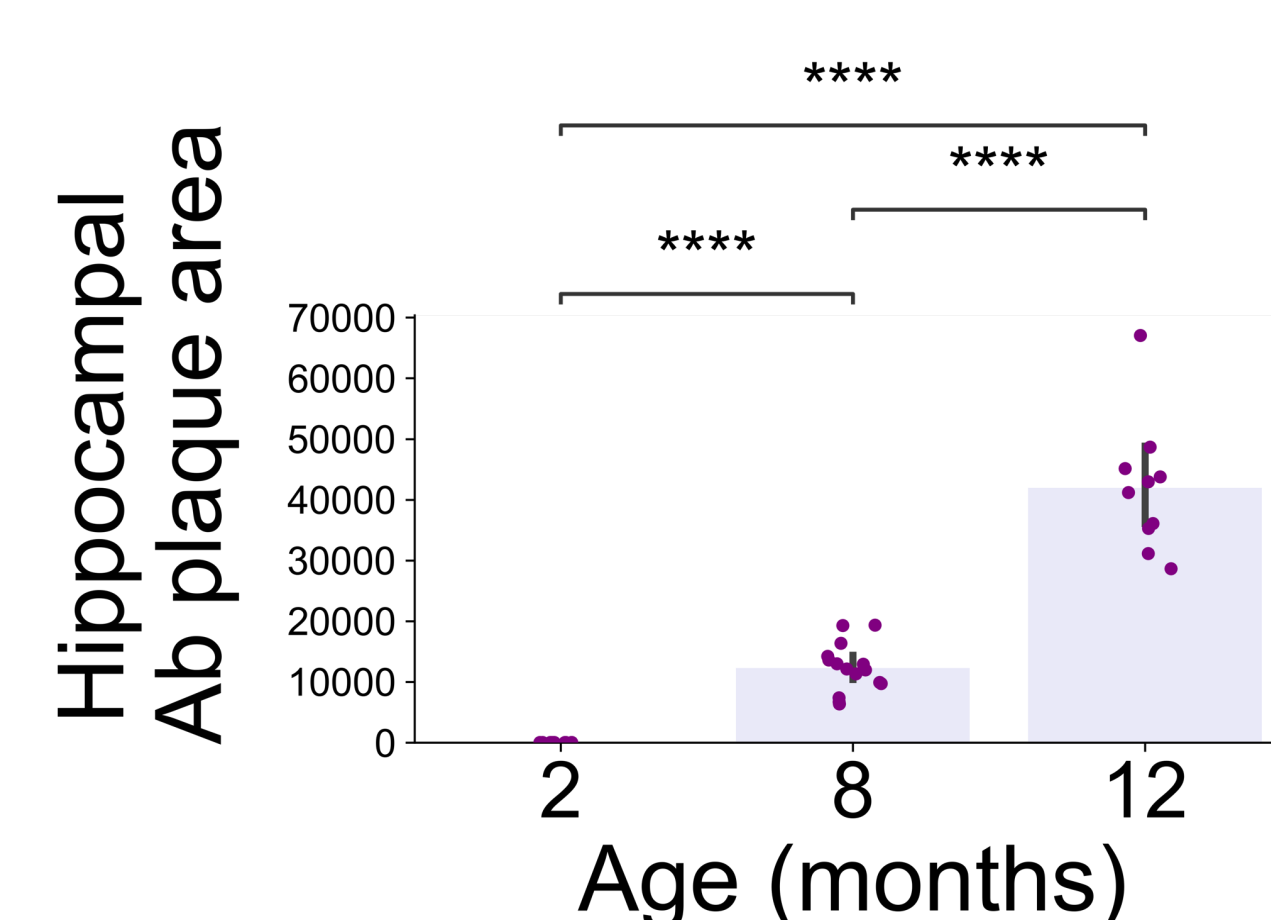


- The Barnes Maze, Novel Object Recognition Test, and T maze were used to evaluate spatial memory function.
- Immunohistochemical staining of beta-amyloid (CT695) and fibrinogen was used to quantify amyloid plaques and BBB leakage, respectively.

Results

Amyloid plaques accumulate throughout the lifespan of AppSAA mice.

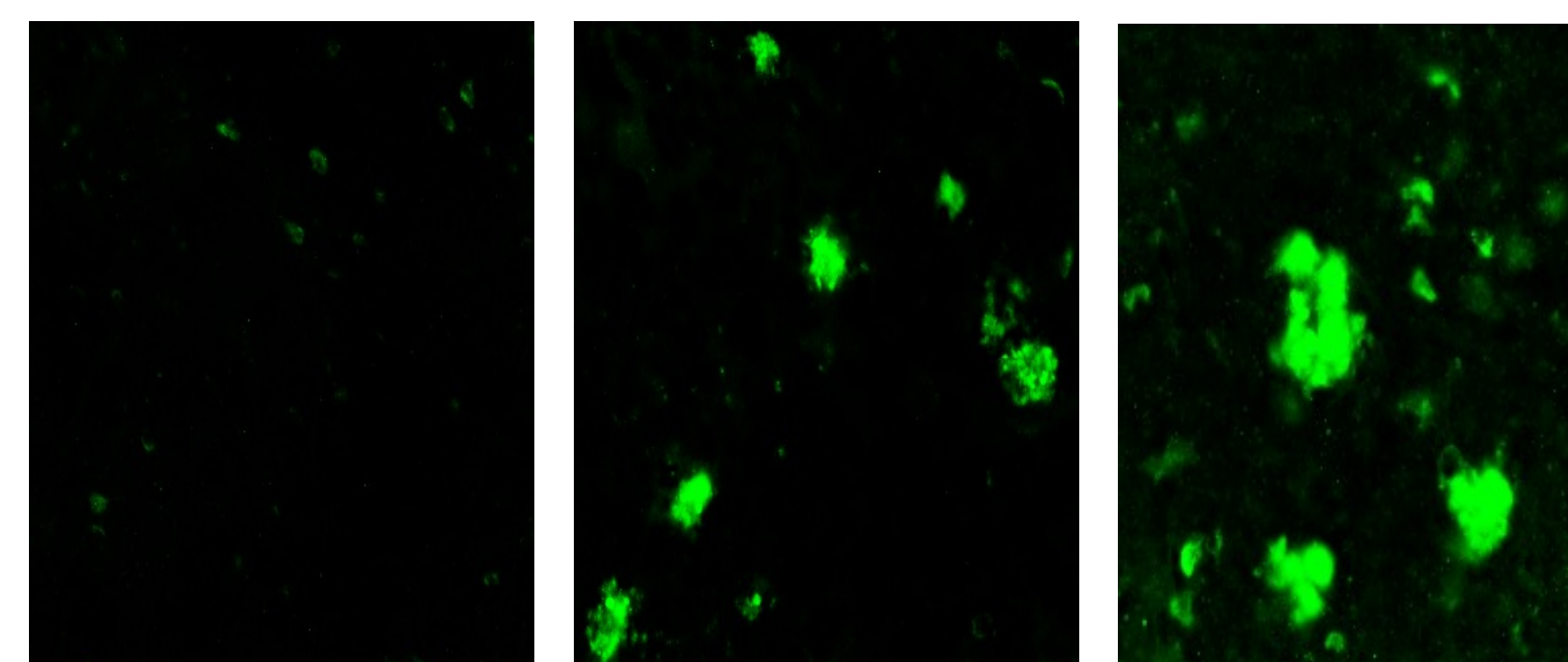
Amyloid load in AppSAA



2mo

8mo

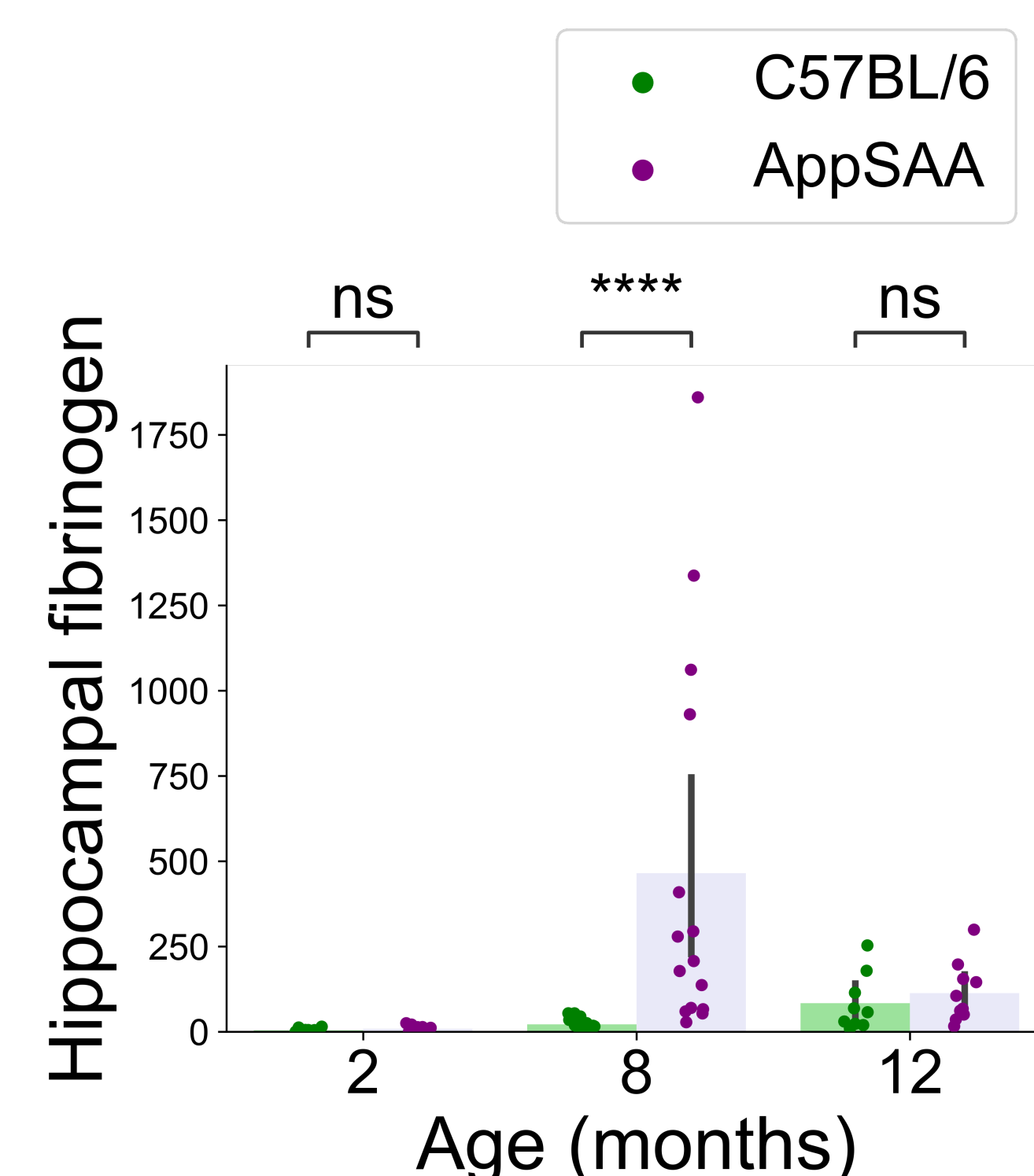
12mo



Amyloid

AppSAA mice have elevated BBB leakage compared to age-matched controls at 8 months but not at 12 months.

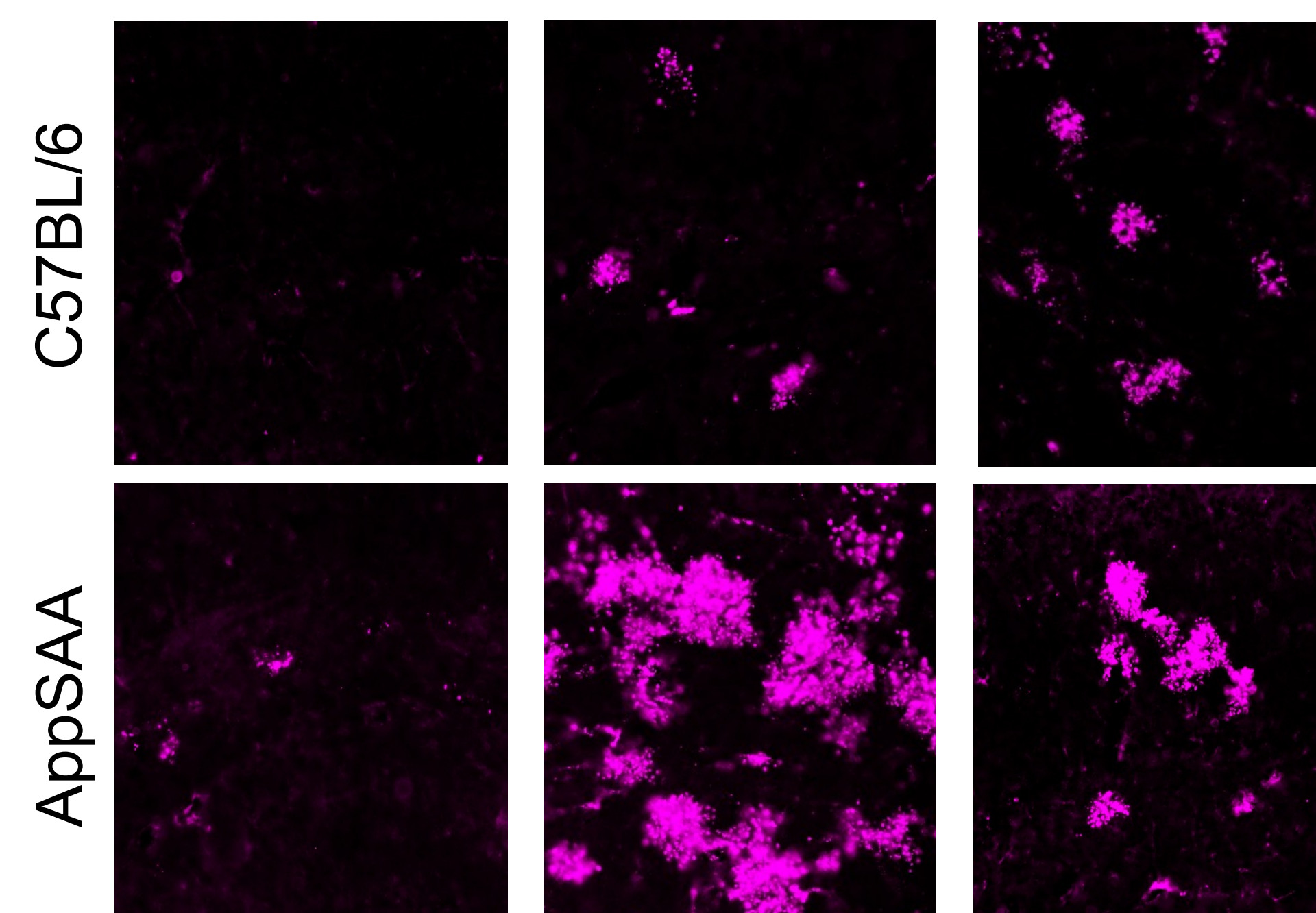
BBB leakage



2mo

8mo

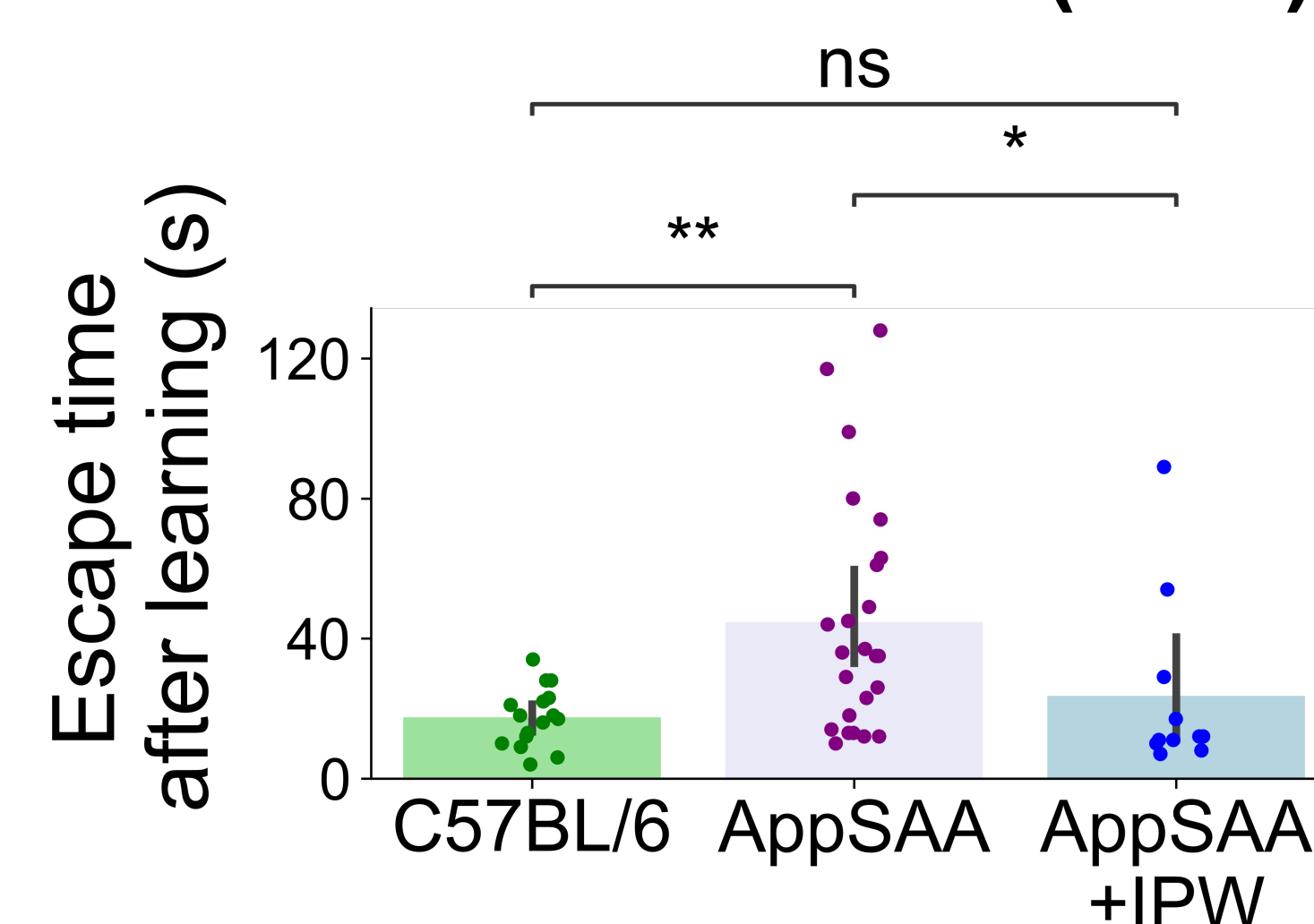
12mo



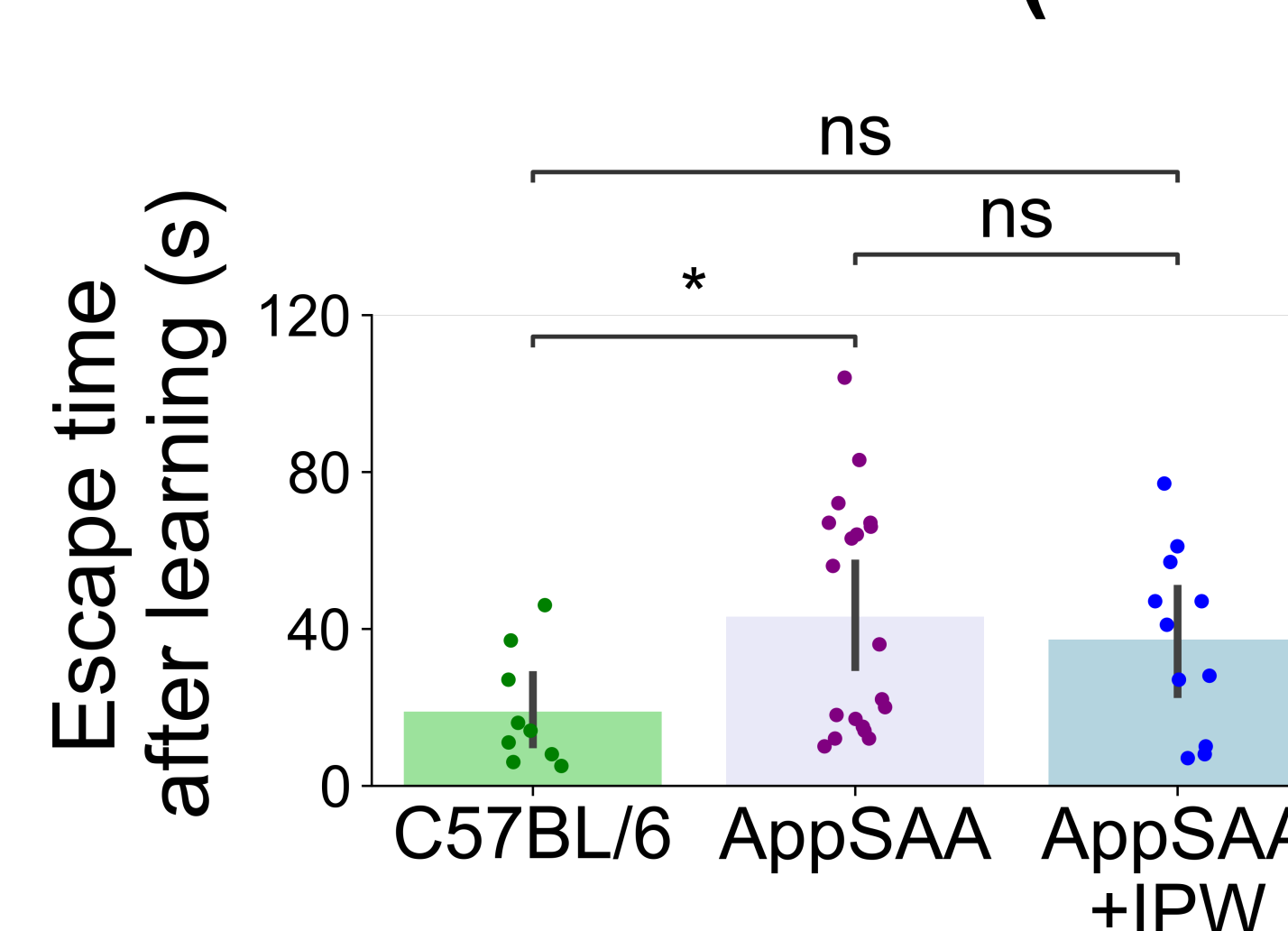
Fibrinogen

IPW treatment in AppSAA mice at 8 months rescues cognitive impairment, but treatment at 12 months does not.

Barnes maze (8mo)



Barnes maze (12mo)



Conclusions

- Amyloid plaques are sufficient to cause BBBd.** AppSAA mice have increased BBBd compared to controls at 8 months, but this difference is attenuated at 12 months.
- BBBd intervention timing is crucial.** Reversal of BBBd with IPW treatment only rescues cognitive impairment in AppSAA mice at 8 months, when leakage is significantly higher than controls.

References

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