

Human Neurovascular Organoids: Uncovering Vascular–Immune Crosstalk in *Alzheimer's Disease*

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TAKE HOME MESSAGE

Neurovascular–immune crosstalk is not a late consequence of Alzheimer's disease but an early, mechanistically central event and human organoid platforms are now powerful enough to model, dissect, and therapeutically target it.



BACKGROUND

Vascular and immune systems contribute to Alzheimer's disease. Animal models and 2D in-vitro approaches poorly reflect neurovascular–immune interactions. Evidence shows the innate immune system and neurovascular networks may impact early disease stages with clinical evidence of vascular dysfunction, BBB disruption and elevated inflammatory markers suggesting these changes occur early, not as later consequences.

METHOD

Stem cell-derived brain organoids enable neurovascular and neuro-immune models with endothelial cells, pericytes, astrocytes, neural networks developed via co-differentiation or fusion & exposed to inflammatory stressors and AD mutations treated with AD patients brain extracts and assessed for BBB integrity, endothelial cell configuration, inflammatory marker expression, microglia activation & amyloid- β or tau-protein accumulation.

RESULT

Organoids recapitulated amyloid- β deposition and tau hyper-phosphorylation, faithfully mirroring features of AD neuropathology.

Endothelial networks showed compromised BBB integrity, high permeability and altered vascular markers reflecting early cerebrovascular changes.

Activated microglia showed robust immune responses coupled with synaptic remodelling, revealing a neuroinflammatory axis central to early AD progression.

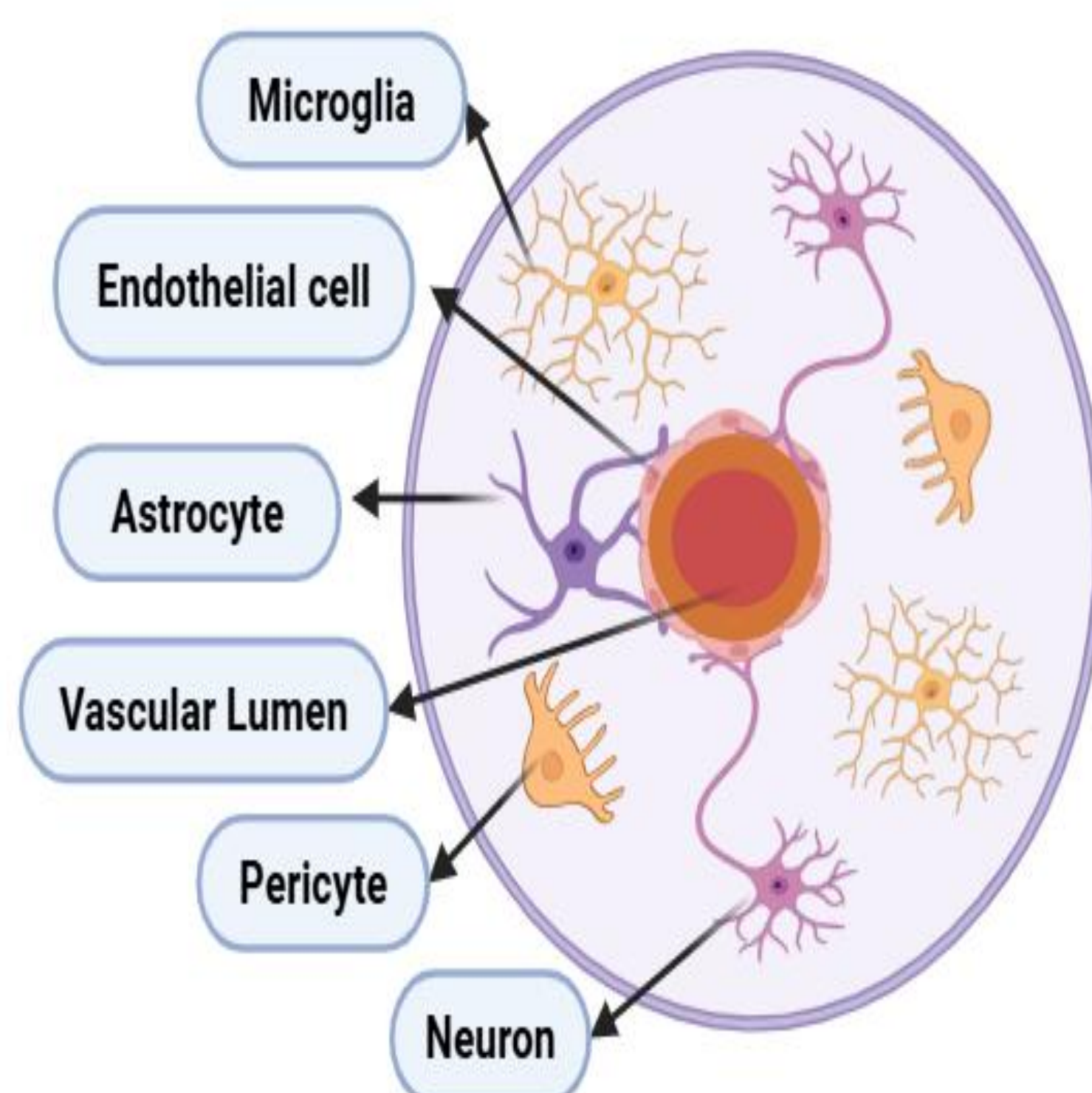
CONCLUSION

The models substantially outperform conventional systems in capturing human-relevant pathophysiology, despite complex challenges it shows promise for advancing disease modeling and therapy targeting neurovascular–immune pathways in AD.

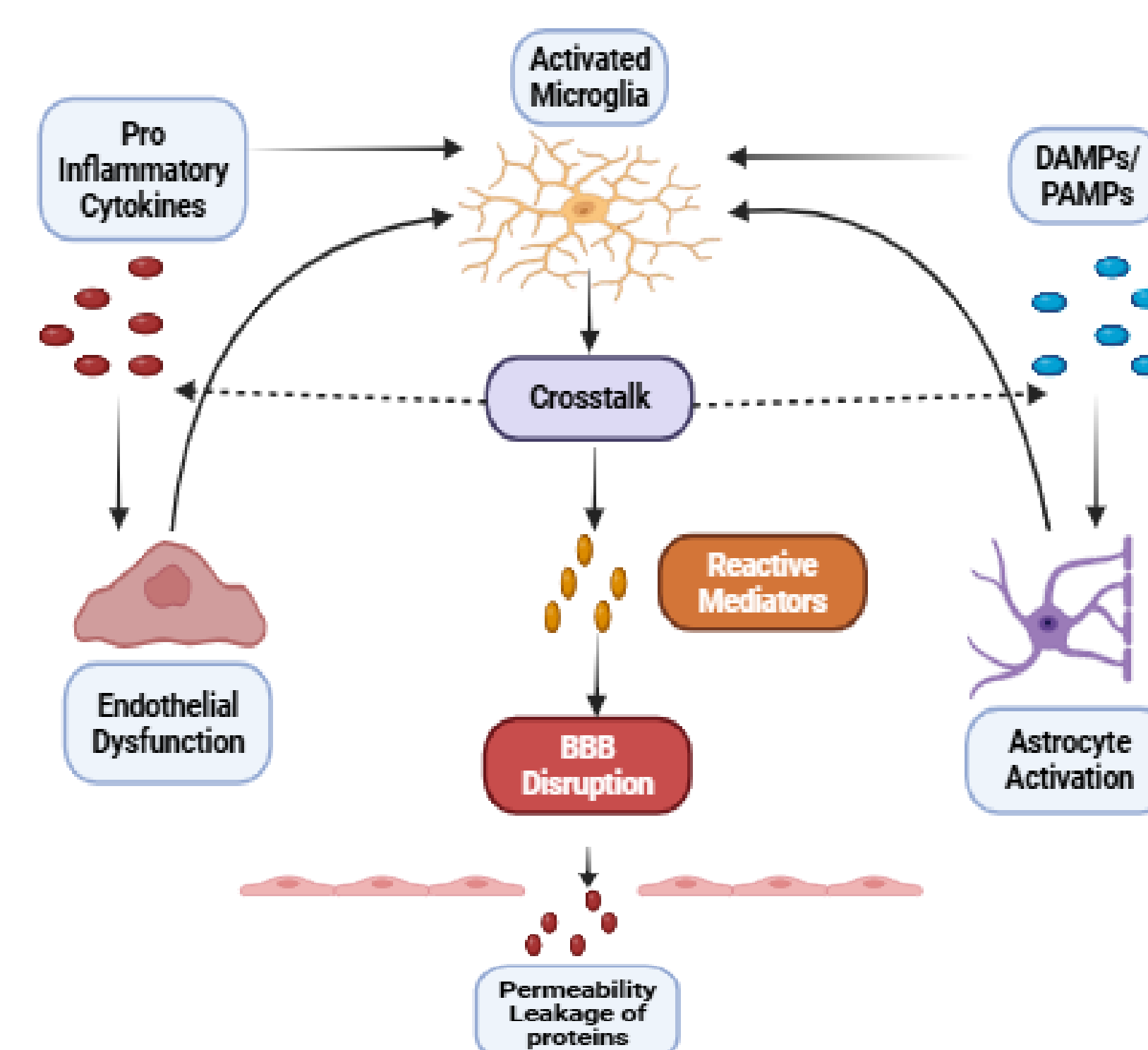
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Neurovascular Organoid Architecture



Vascular-Immune Crosstalk in AD



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