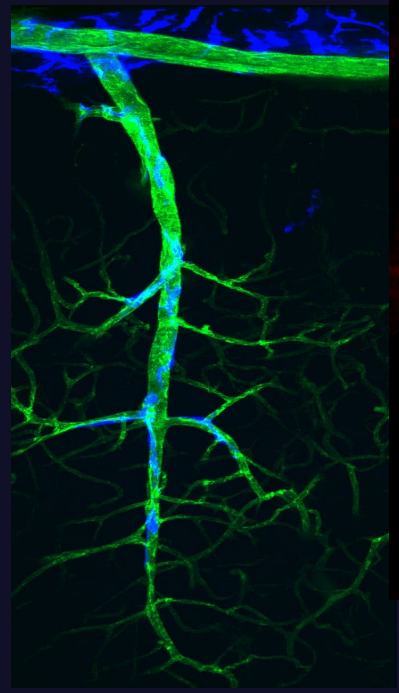
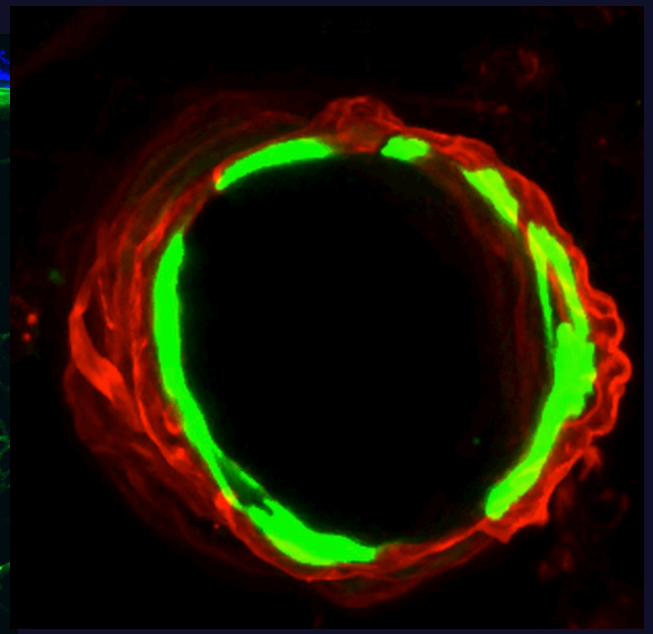
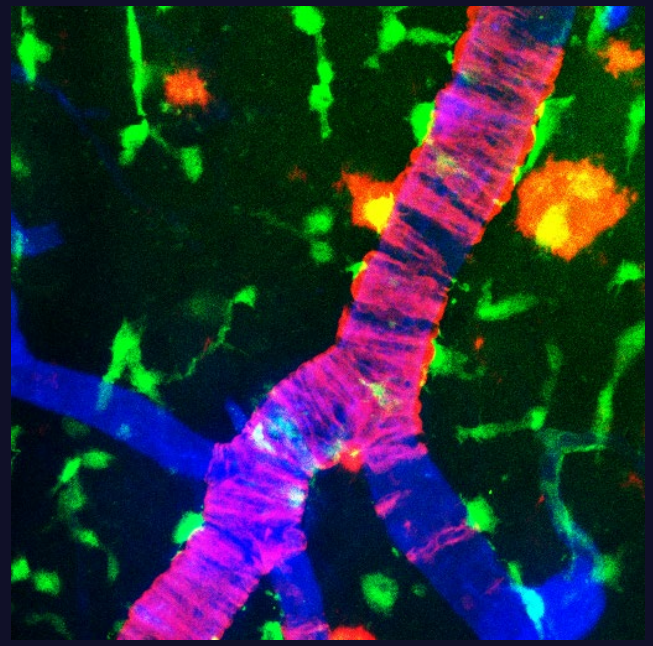
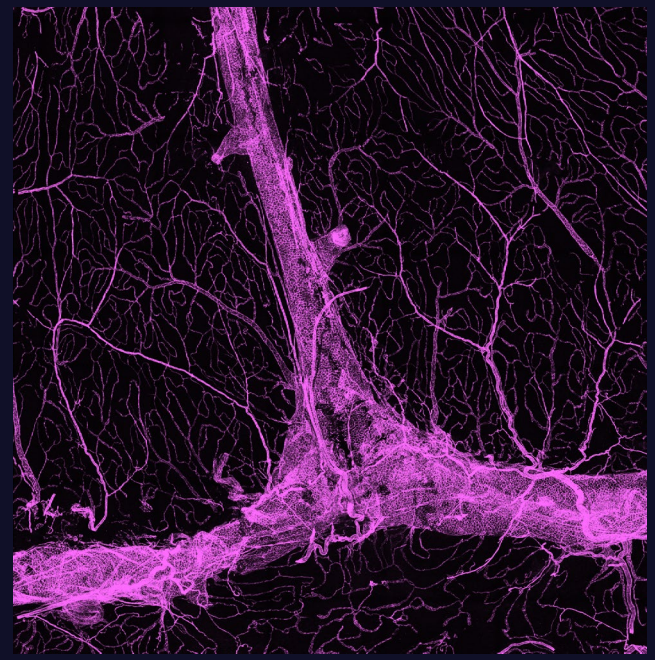
Brain-body crosstalk and brain health: neurovascular, immune, and endocrine interfaces

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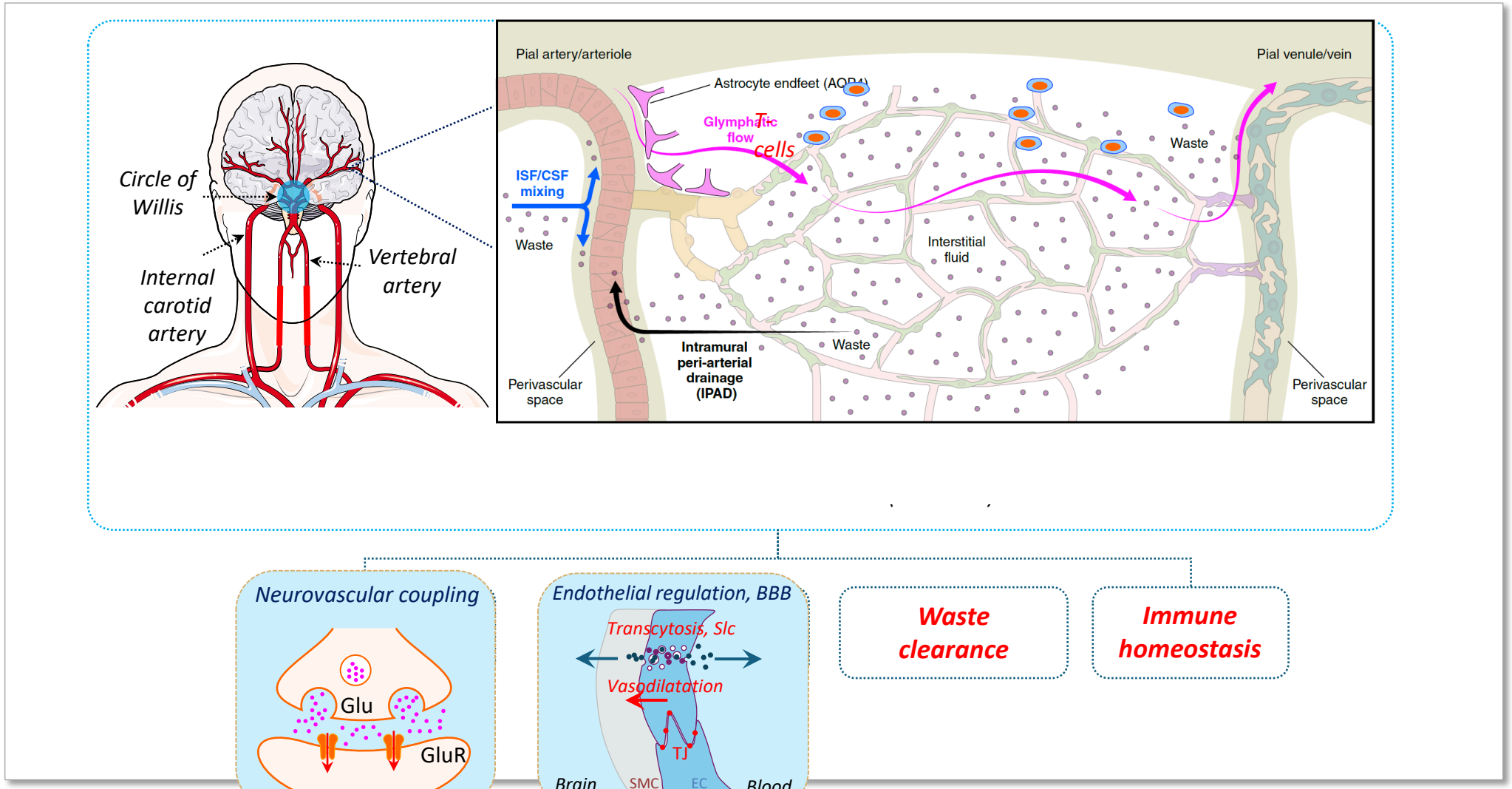
Outline

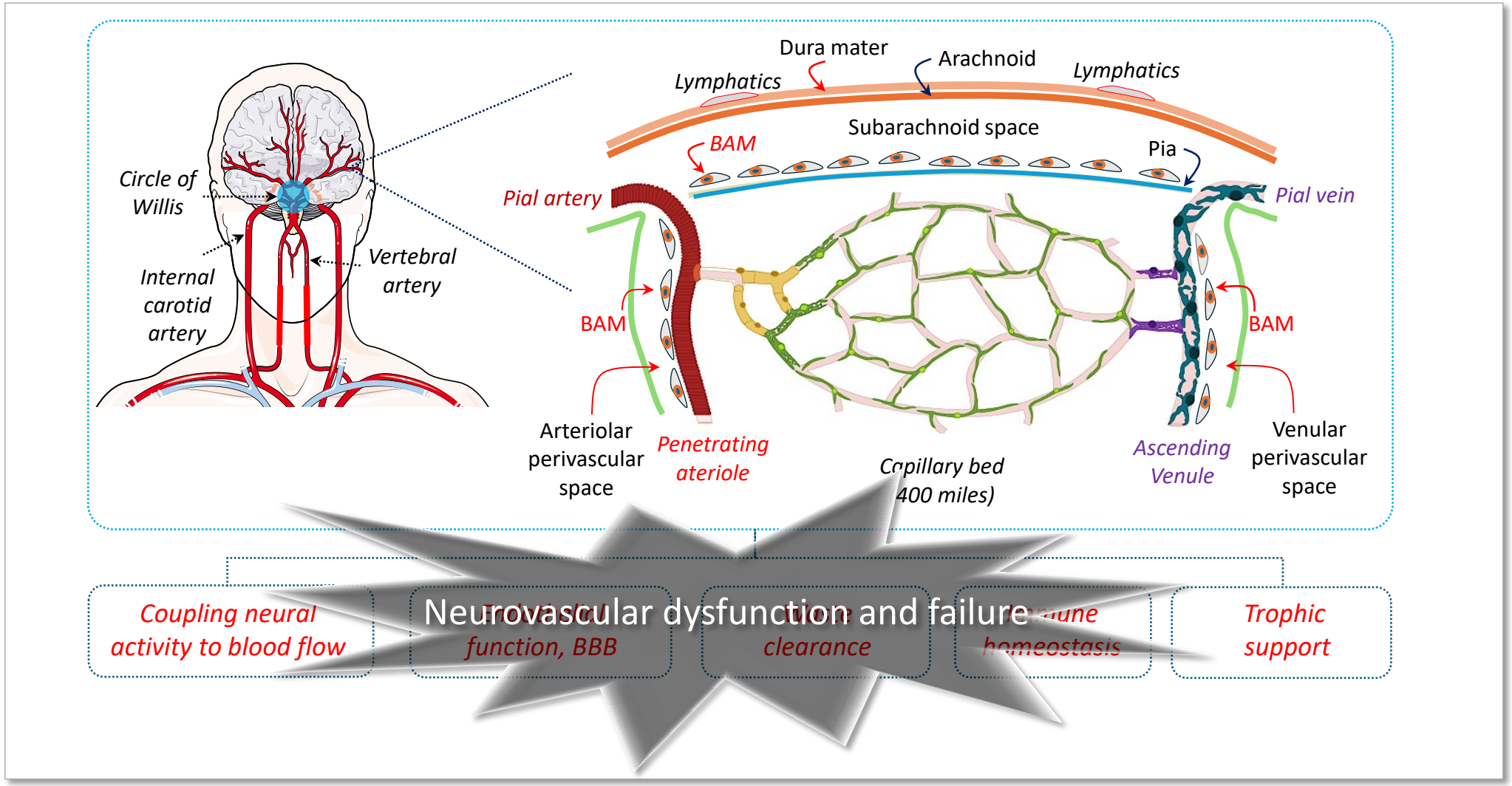
- Neurovascular and neuroimmune interactions in brain health
- Systemic influences on ischemic brain injury and stroke recovery
- Body-brain crosstalk in cognitive impairment in hypertension
- Prospects for diagnostic biomarkers and therapeutic targets

Brain health depends critically on neurovascular health



Santisteban and Iadecola, *Neuron, 113:49, 2025*

Neurovascular dysfunction is a major threat to brain health



Neuron, 113:49, 2025

The neurovascular insufficiency spectrum

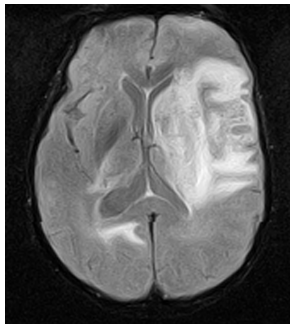
Thrombosis, cardiac embolism

↓

Ischemic cascade

↓

Ischemic stroke



<u>In the US</u>

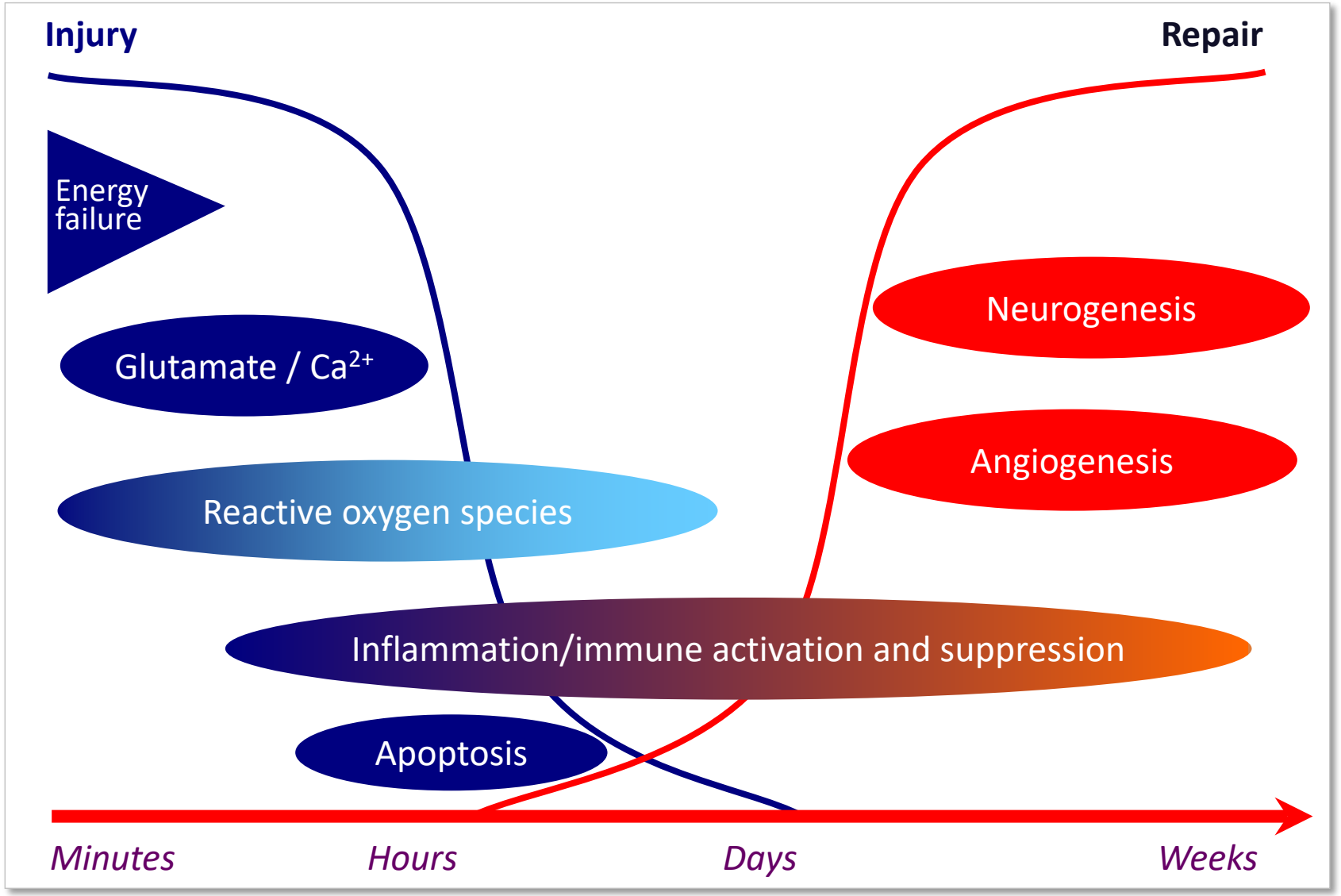
1 stroke/40 sec

≈800,000/year

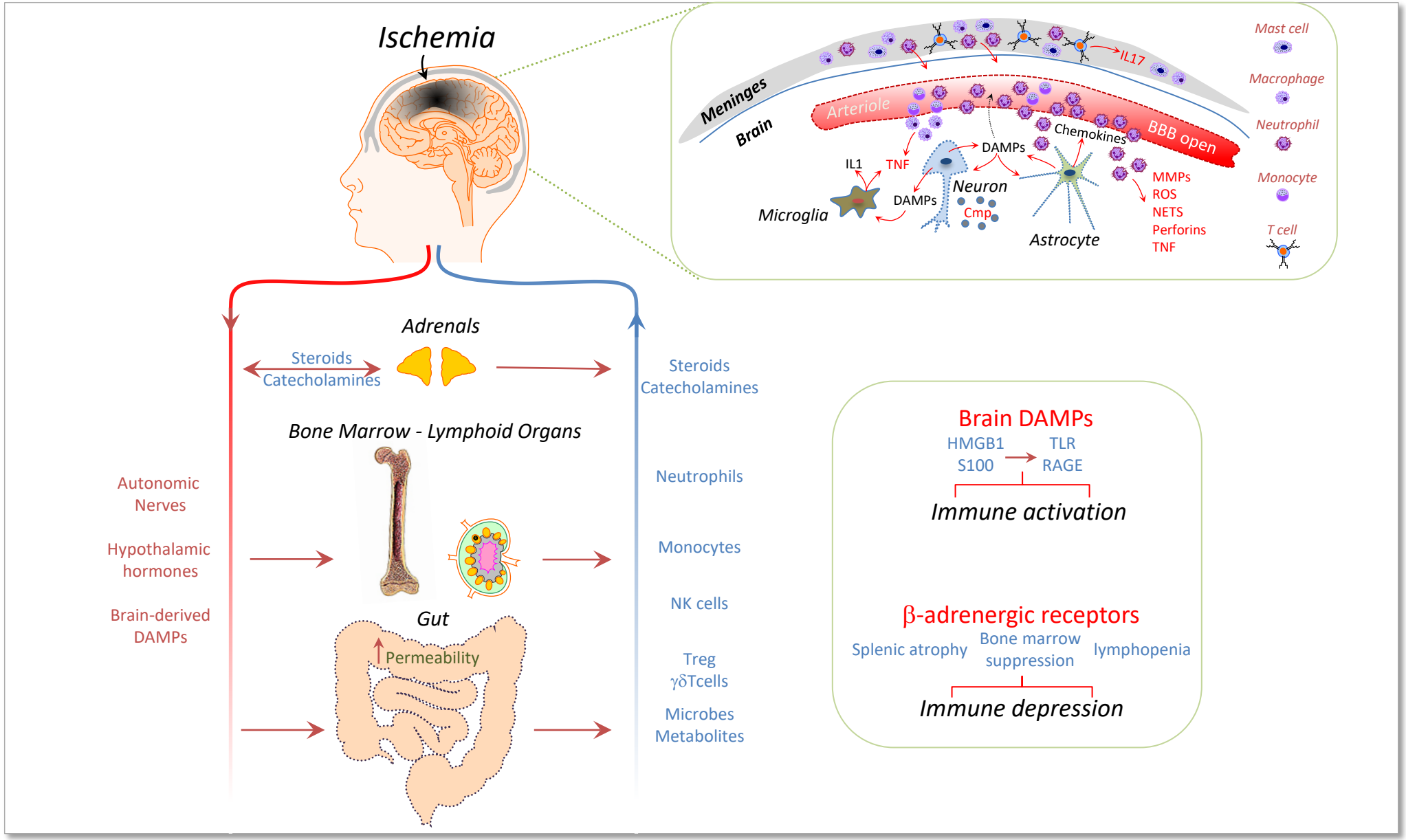
5th cause of death

Iadecola and Anrather, *Immunity, 58:18, 2025*

Inflammation and immunity in cerebral ischemic injury

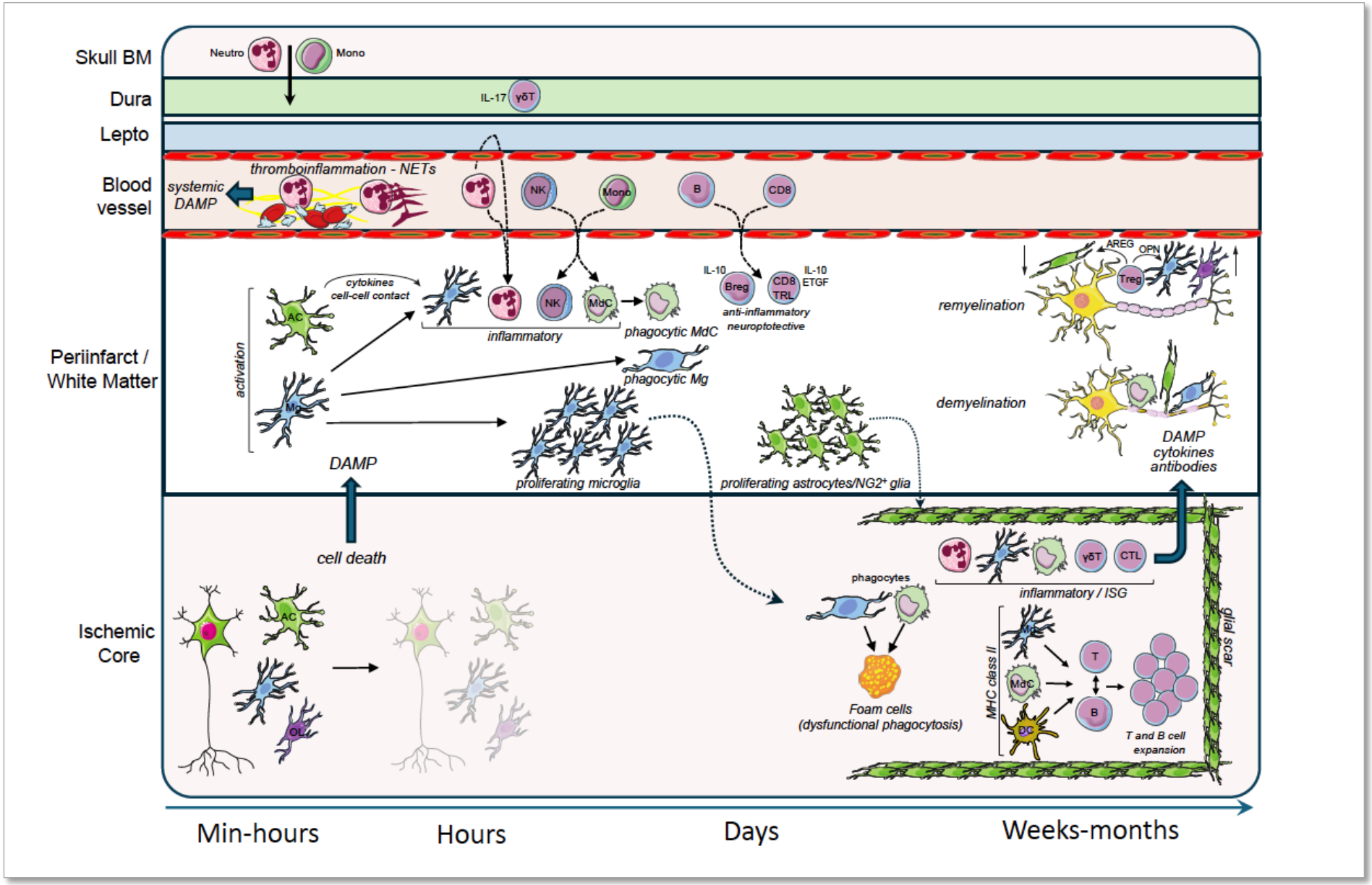


The brain-body interface in ischemic stroke: damage



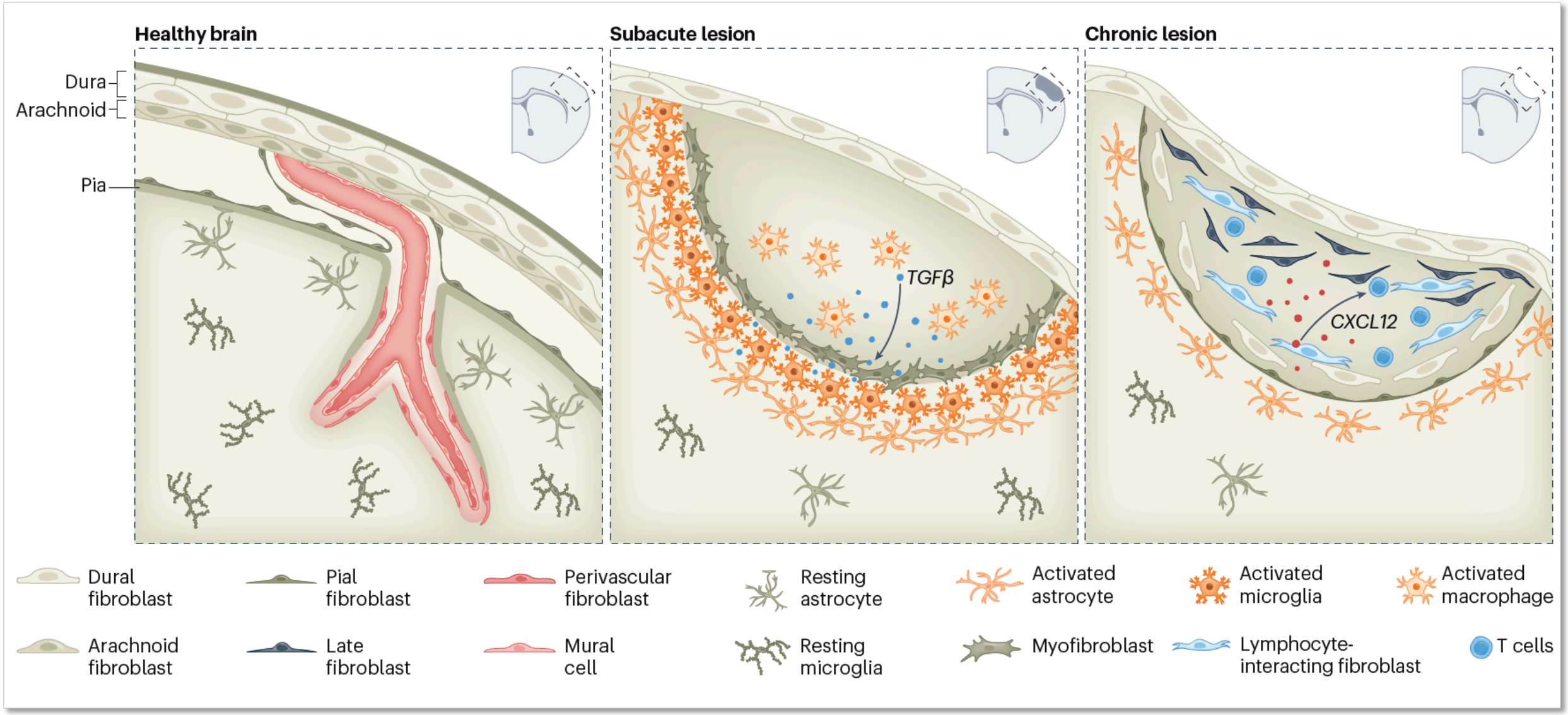
Iadecola., et al., *JCI, 130:2777, 2020*

The brain-body interface in ischemic stroke: recovery



Garcia-Bonilla et al., *Nat. Immunol, 2024; Immunity, 58:18, 2025*

The brain-body interface in ischemic stroke: recovery



Garcia-Bonilla et al., *Nat. Immunol, 2025;* Ewing-Crystal et al. *Nature, 2025*

The neurovascular insufficiency spectrum

Vascular dysregulation

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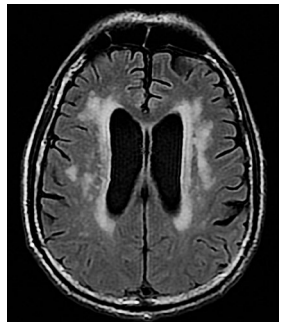
Neurovascular failure

↓

Cognitive impairment



Vascular cognitive impairment

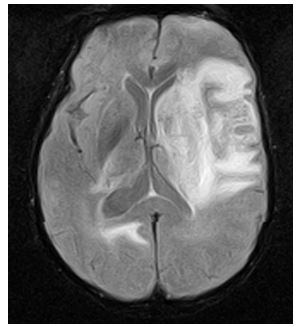
Thrombosis, cardiac embolism

↓

Ischemic cascade

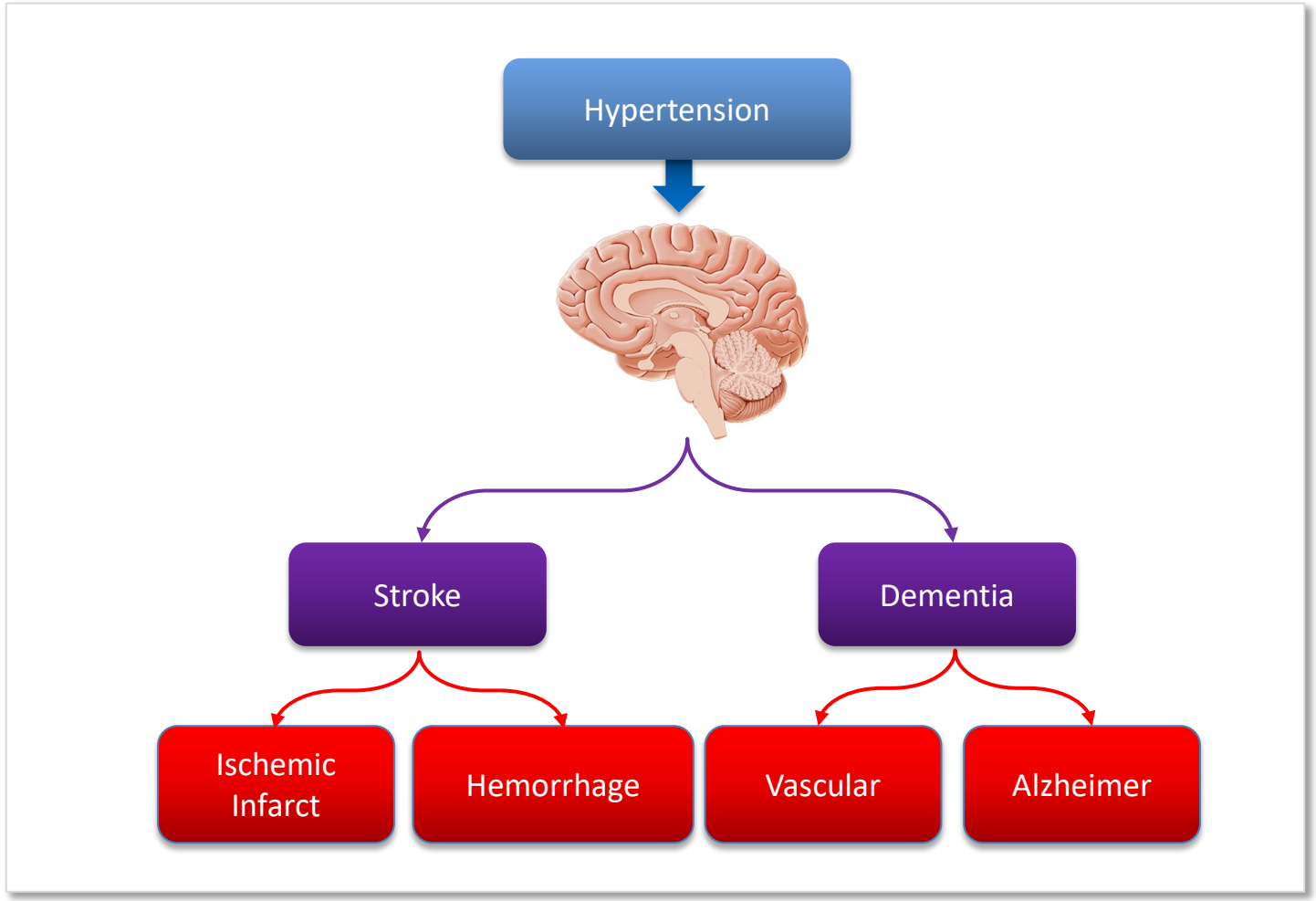
↓

Ischemic stroke



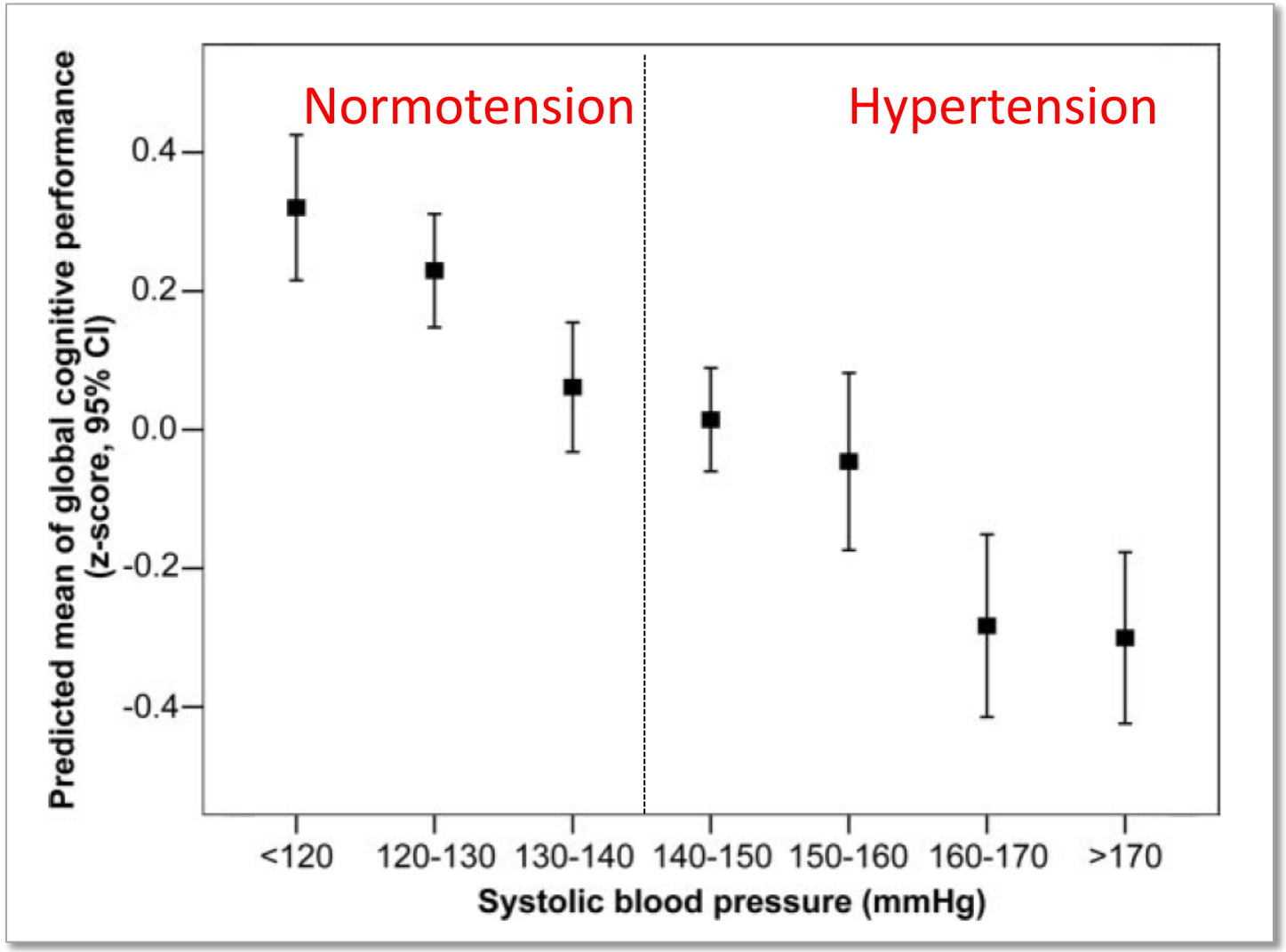
Immunity, 58:18, 2025

Hypertension affects 1.3 billion people worldwide and is a leading risk factor for stroke and dementia including AD



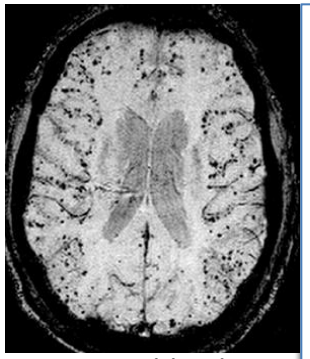
Iadecola and Davisson, Cell Metab 2008

Harmful effects of hypertension on cognition: The SEARCH-Health study

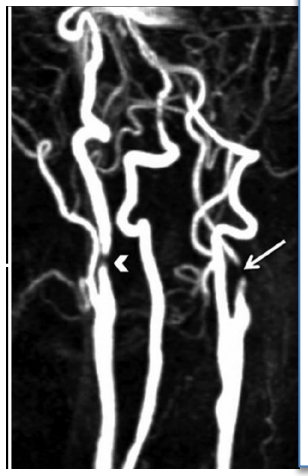


Knecht et al., *Hypertension 51:663, 2008*

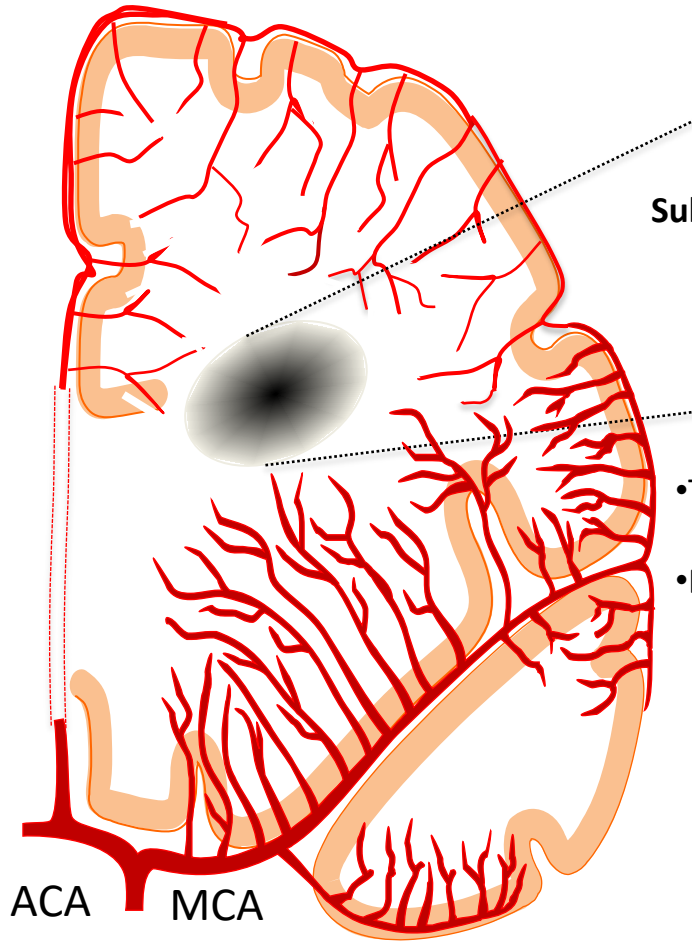
Damaging effects of hypertension on the brain



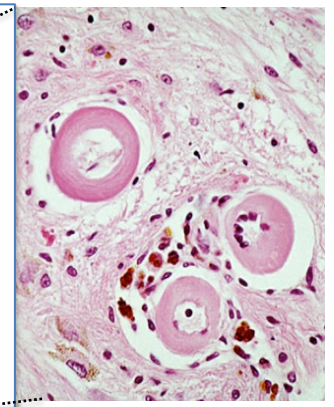
Microbleeds



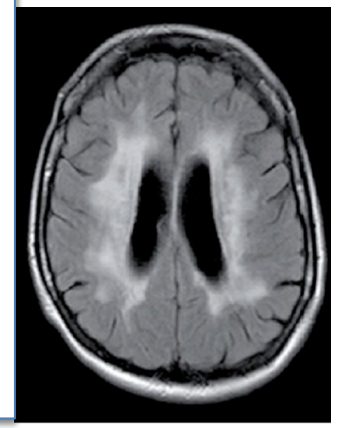
Bilateral carotid stenosis



Modified from: *Iadecola, Neuron, 2013*

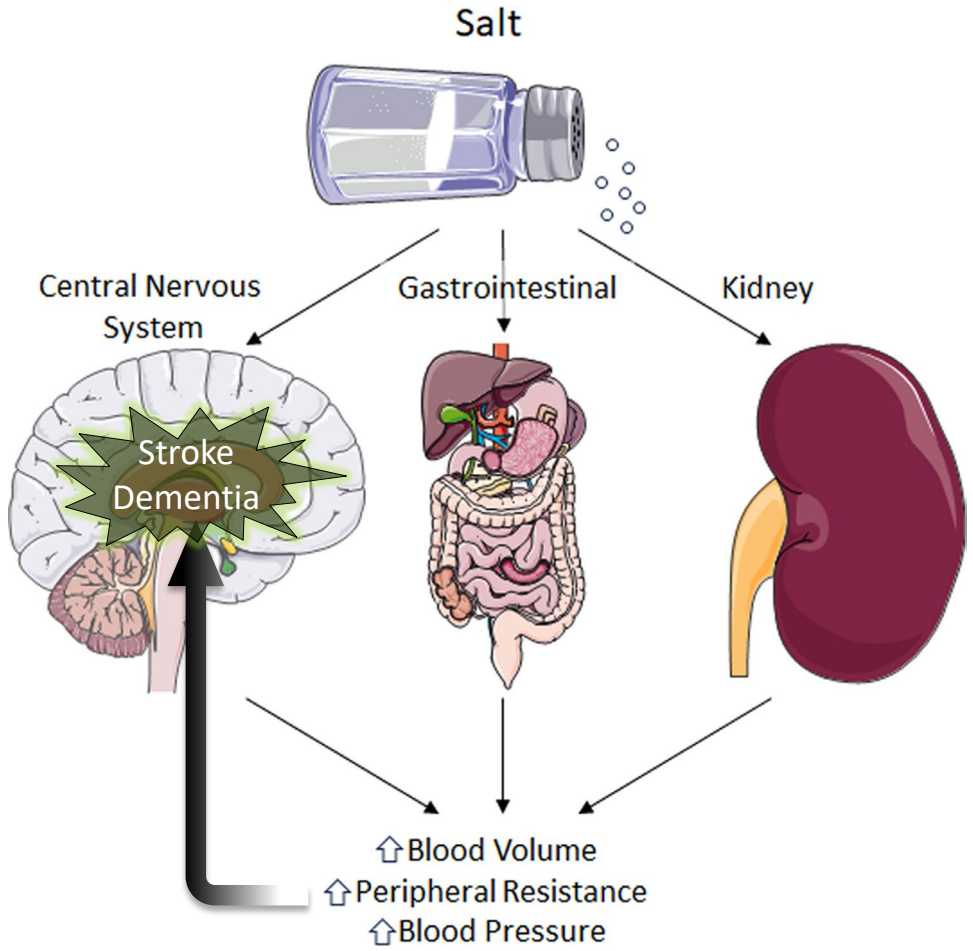


Lipohyalinosis



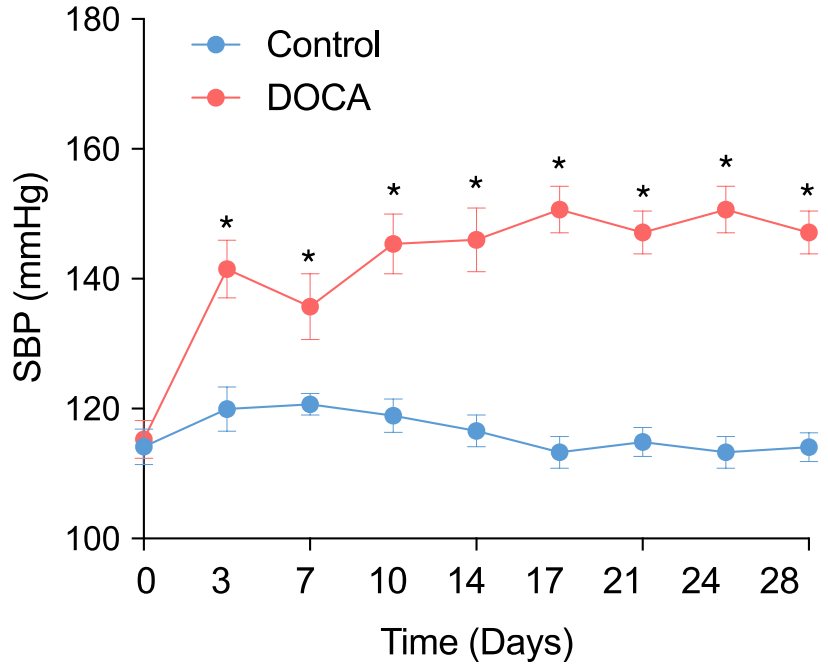
White matter damage

Body-brain crosstalk in salt-sensitive hypertension



Stoker et al. Hypertension, 2024

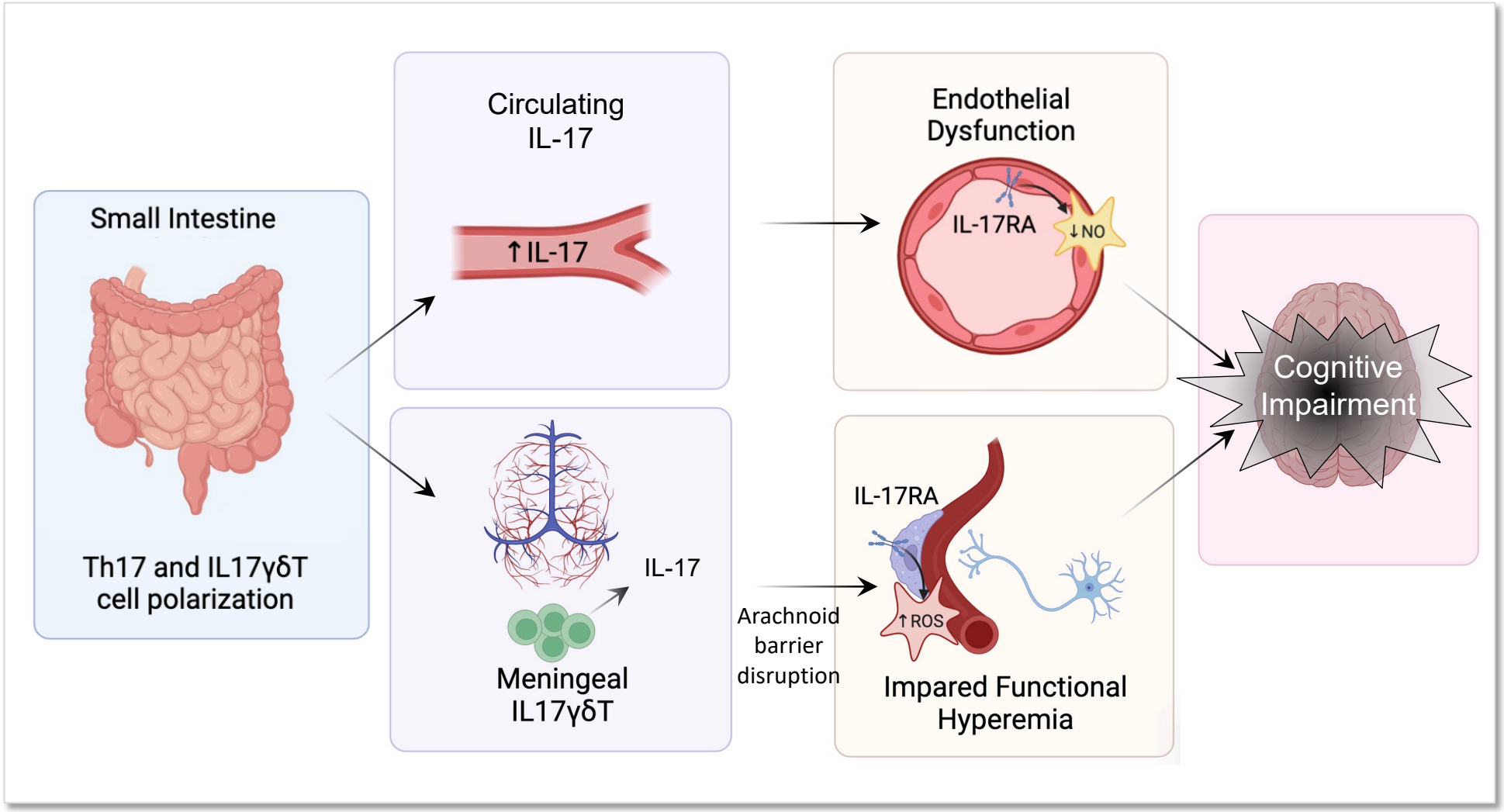
Monica Santisteban



Salt-sensitive hypertension (50% of cases):

- Resistant to treatment, most common in minorities
- Doubles the the risk of cardiovascular events including stroke and dementia

Body-brain crosstalk in the cognitive dysfunction of salt-sensitive hypertension



Santisteban et al., Nat Neurosci, 27:63, 2024

Summary and Conclusions

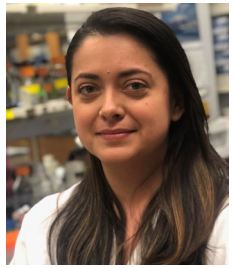
- Crosstalk between the neurovasculature and systemic immunity plays a critical role in both maintaining brain health and promoting disease.
- In stroke, systemic factors not only exacerbate acute brain injury but also play essential roles in brain repair.
- In hypertension, interactions between systemic immune cells and the neurovasculature impair brain resilience and lead to cognitive decline.
- These body-brain interactions present promising avenues for the development of novel biomarkers and therapeutic strategies.
- A nuanced understanding of these complex, and sometimes double-edged, processes is key to unlocking their benefit to brain health."

Collaborators


J. Anrather


L. Park


G. Faraco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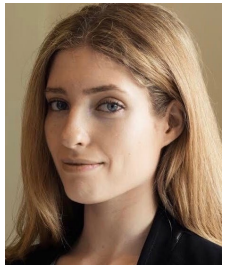
Vanderbilt U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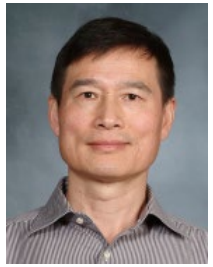
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NIH

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American Heart Association | American Stroke Association

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