

A Literature Review Evaluating The Impact Of Pericytes On Blood Brain Barrier Function In Alzheimer's Disease

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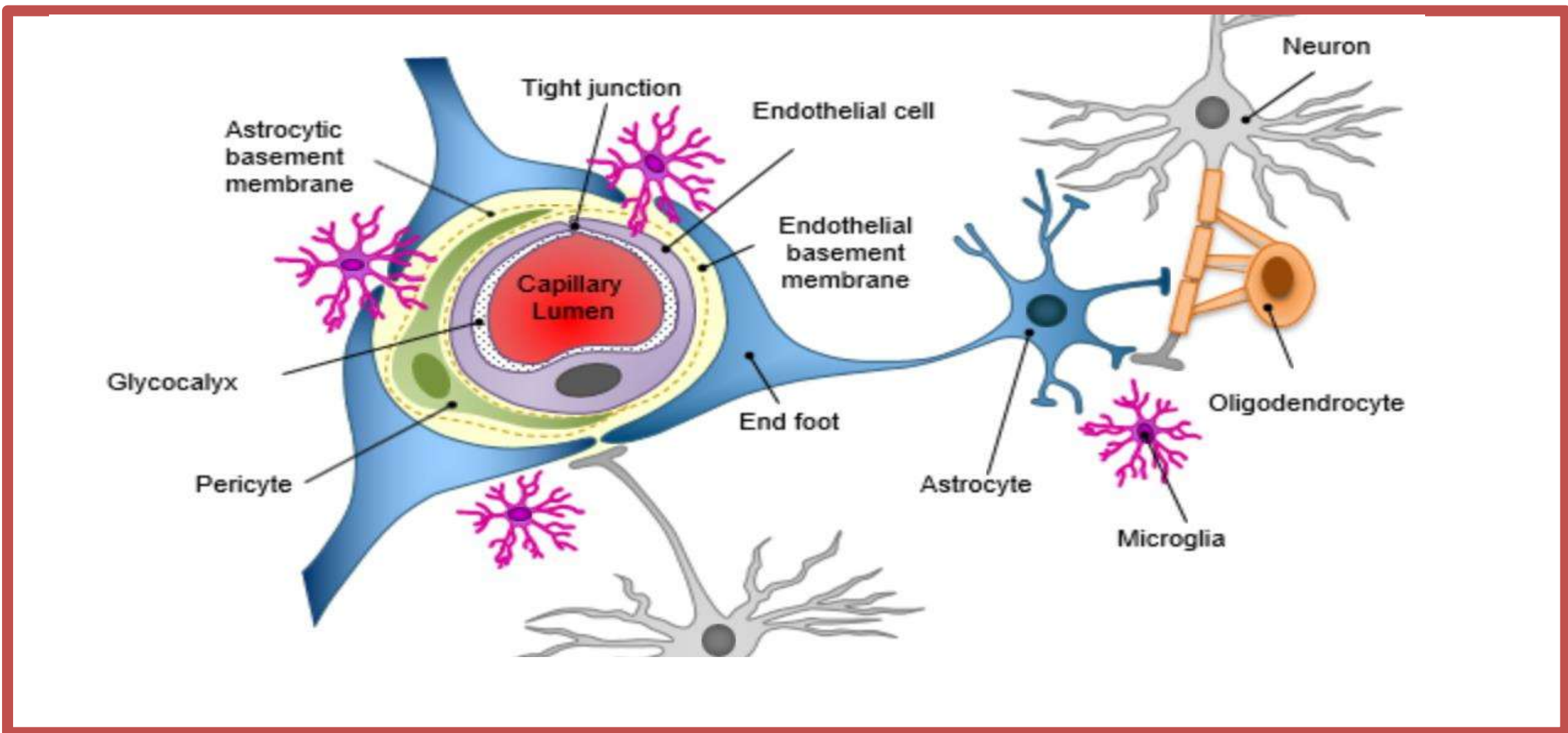
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Background

Pericytes are a significant component of the neurovascular unit and are critically located in the basement membranes between the brain capillary wall and astrocyte end feet (Fig. 1). In the healthy adult brain, they are crucial in maintaining blood-brain barrier (BBB) integrity, regulating cerebral blood flow, and clearing brain waste. Pericyte loss occurs in normal ageing but in Alzheimer's disease (AD), which is a disease characterized by declining cognition and memory, degeneration and loss occur at a much greater frequency.

Figure 1: Location of pericytes and surrounding cells and structures in the neurovascular unit



Objective

The objective of this literature review was to determine the impact of pericyte degeneration and loss in AD pathogenesis.

Methods

To identify primary research papers that described pericyte involvement in AD, a literature review using PubMed and Ovid databases was conducted. The search terms used included pericytes, pericyte loss, blood-brain barrier, hypoperfusion, clearance, and Alzheimer's disease. Publication date range was 2012-2024. Eight primary research papers were selected for evaluation.

Result

The findings from the eight primary research papers (see References) indicated that pericyte degeneration and loss contribute to three key features of AD pathogenesis:

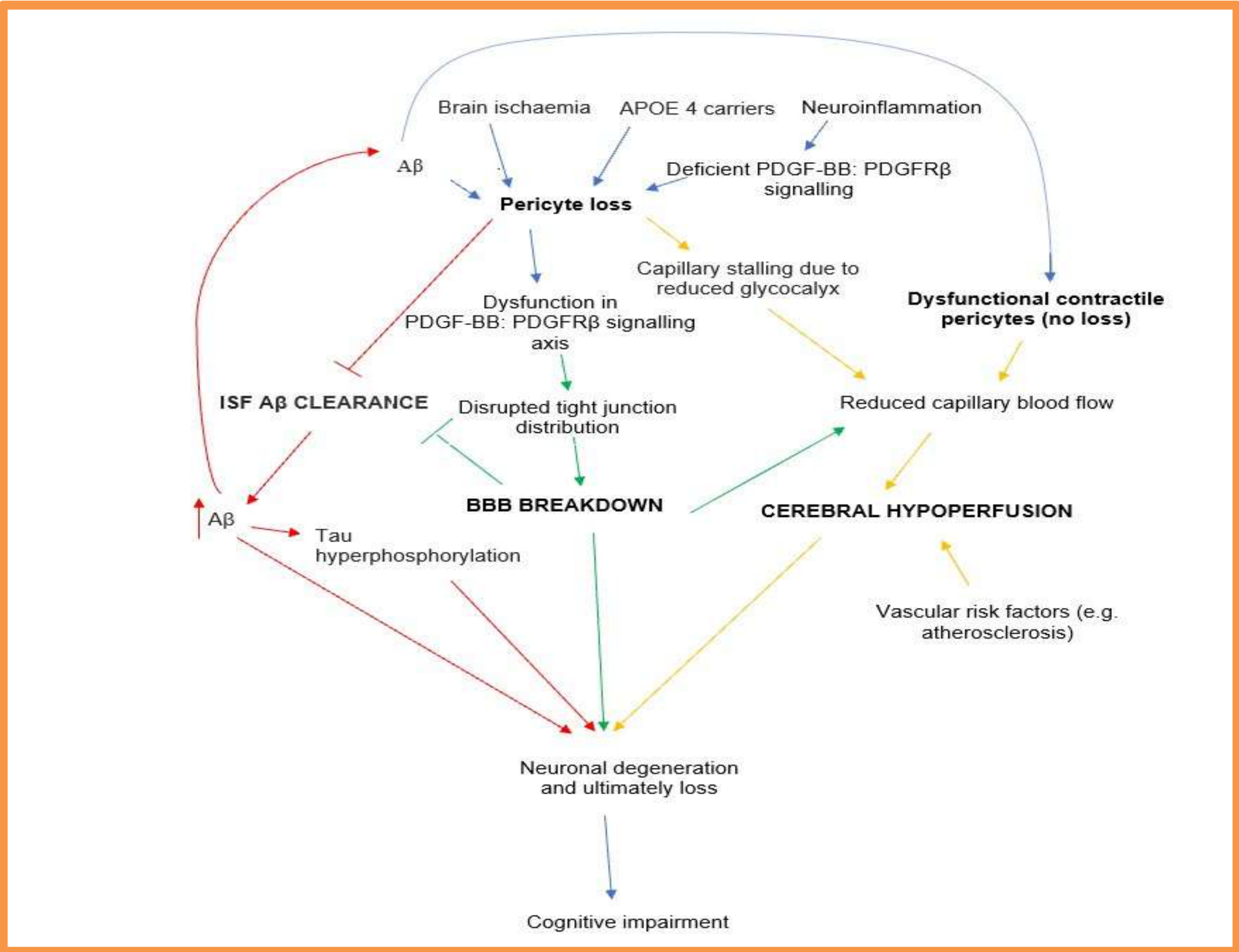
- 1) BBB breakdown:** The breakdown of the BBB appears to be associated with the degeneration of pericytes(1,2). The result of this breakdown is increased permeability of neurotoxins, which cause and exacerbate neuronal damage.
- 2) Reduced cerebral blood flow:** Pericyte loss and A β stimulation of contractile pericytes leads to reduced capillary blood flow(3,4,5), which is associated with cognitive impairment by leaving brain tissue hypo-perfused.
- 3) Impaired A β clearance:** Pericyte loss impairs A β clearance, by proposed mechanisms of disrupted phagocytic activity mediated by LRP-1 and dysregulation of the intramural periaxonal drainage and glymphatic drainage pathways(6,7,8). This leads to an acceleration of A β and tau accumulation in the brain resulting in neuronal injury, synapse loss and associated cognitive impairment.

Figure 2 illustrates these findings and their interconnectedness.

Discussion

Multiple methods confirmed the involvement of pericyte degeneration and loss in AD. These methods include the use of human brain imaging studies(1,2), in vitro human and mice brain cell studies(3,5) and transgenic animal studies(6,7). Limitations include the use of participants in human studies without a diagnosis of AD(1) and the use of transgenic pericyte deficient mice models to reflect the human disease process(6). To improve, different mice models, more tests of cognition and longitudinal studies following participants, and their potential disease progression might be considered.

Figure 2: Impact of pericyte loss on AD pathogenesis



Conclusion

Primary research papers were identified that confirmed the involvement of pericyte degeneration and loss in the pathogenesis of AD (Figure 2). Pericyte degeneration and loss are significant factors to consider in the progression of AD. Attempts have already been made to restore pericyte function to prevent and treat AD (9). The results of this literature review confirm that pericytes are an important therapeutic target of the future and warrant further investigation.

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