

Pulse pressure: A game changer in the fight against dementia

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A recent paper published in *Frontiers in Neuroscience*, outlines a pulse-pressure-induced pathway of cognitive decline that sheds light on why previous treatments for dementia may have failed and proposes promising new directions for the prevention and treatment of dementia.

"Over the last couple years, a sea change in [dementia](#) and Alzheimer's disease research has occurred. Focus has shifted from solely targeting [amyloid-beta](#) in the brain to the opinion that more fruitful progress could be made by addressing factors that compromise the [blood brain barrier](#)," explains co-author Mark Carnegie, of The Brain Protection Company based in Australia. "Elements of the constellation include chronic age-related inflammation, genetic predisposition, and cardiovascular abnormalities, notably high blood [pulse pressure](#)."

Connecting a large and rapidly growing body of evidence, the researchers elucidate how elevated pulse pressure may cause dementia. Pulse pressure is the difference between systolic and [diastolic blood pressure](#) and commonly increases with age.

The researchers propose that elevated pulse pressure in blood traveling to the brain can cause inflammation, [oxidative stress](#), mechanical stress, cellular dysfunction, and [cell death](#) in the blood brain barrier that leads to brain damage.

The link between blood brain barrier breakdown and dementia is intuitive, as the blood brain barrier has specifically evolved to support and protect delicate brain tissue by keeping circulating cells, pathogens, and other unhealthy substances in blood from infiltrating the brain. There is significant evidence supporting that disruption of the blood brain barrier is a key driver of cognitive decline and dementia.

Senior author of the paper, Prof. David Celermajer of The Brain Protection Company, says that "this is an important paradigm shift in our understanding of the pathogenesis of dementia."

He further adds that "although there are likely several causes of blood brain barrier disruption, recent human cell culture experiments, animal models, and epidemiological evidence have pointed to high blood pulse

pressure as one potential key cause."

Pulse pressure may therefore be a promising new therapeutic target for preventing or slowing cognitive impairment, which gives new hope in the fight against dementia.

Moreover, the authors discuss how elevated pulse pressure may have also prevented previous treatment strategies from working optimally against dementia.

For the past two decades, a primary focus of drug development for Alzheimer's disease, the most prevalent form of dementia, has been to target the molecule amyloid-beta. However, despite billions of dollars spent on R&D, that approach has yet to be successful.

The researchers suggest that targeting amyloid-beta alone to treat dementia may be an uphill battle since concurrent elevated pulse pressure will continue to activate secretion of various inflammatory and oxidative molecules and amyloid-beta from the blood brain barrier into brain tissue.

Also, stem and progenitor cell therapies have gained significant attention as potential strategies to repair blood brain barrier damage and treat dementia, but chronic inflammatory and oxidative stress due to elevated pulse pressure can impact the health of stem and progenitor cells.

Dr. Rachel Levin, lead author of the paper, says that "combination therapy has been paramount in the treatment of other challenging diseases, in particular cancer. Therefore, in dementia, reducing elevated pulse pressure could prove to be synergistic with other therapeutic approaches such as anti-amyloid-beta drugs or stem cell therapy."

The authors issue a call to action for academic and industry leaders to

develop novel drug candidates or devices that reduce elevated pulse pressure and progress them to clinical trials. Celermajer states that "strong [animal model](#) data already supports the role of high pulse pressure in [blood brain](#) barrier disruption and dementia pathology; now more human studies are needed."

More information: *Frontiers in Neuroscience* (2020). [DOI: 10.3389/fnins.2020.00669](#) , [www.frontiersin.org/articles/10.3389/fnins.2020.00669/full](#)

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