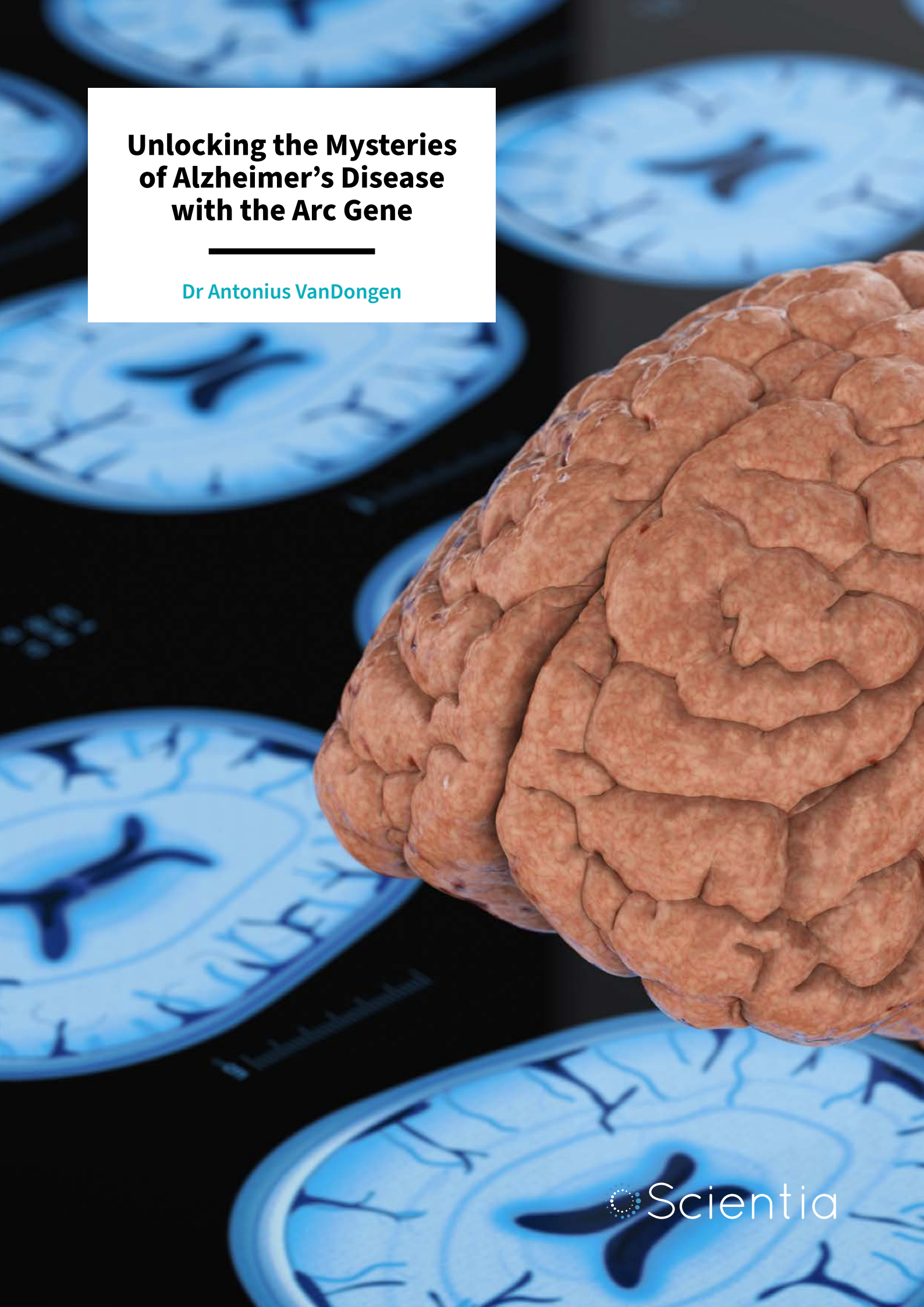
Unlocking the Mysteries of Alzheimer's Disease with the Arc Gene

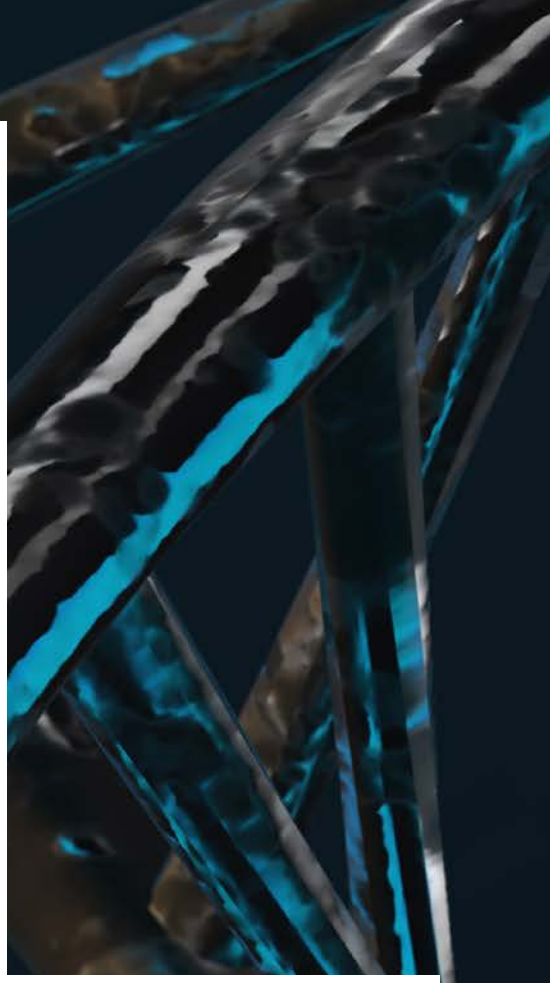
Dr Antonius VanDongen



Scientia

UNLOCKING THE MYSTERIES OF ALZHEIMER'S DISEASE WITH THE ARC GENE

Our vulnerability to developing diseases and conditions depends upon a complex interaction between our genes, lifestyle, and environmental factors. Alzheimer's disease is no exception to this, and sadly, it remains without a cure. **Dr Antonius VanDongen** and his team from Duke University are studying the mechanisms underlying learning and memory, specifically focusing on the activity-regulated cytoskeletal memory gene Arc. Their work is driving forward our understanding of the memory problems that characterise Alzheimer's disease.



Upkeeping Memories: The Process of Memory Consolidation

Memory consolidation is the process by which our brains store and strengthen newly acquired information. It happens after we learn something or experience a new situation. This information first enters short-term memory. Then, the connections between brain cells representing this specific memory are strengthened. As these connections strengthen over time, the information is transferred to long-term memory, where it is stored and solidified.

Imagine your brain as an extensive library of books, each representing a memory. When you experience something new, your brain starts writing a new book for its library. Memory consolidation is a process in which the brain ensures the books in the library are well organised. If you repeatedly encounter a similar memory, the draft of that book becomes better and better. This revision process uses all the resources the brain has to offer (such as previous memories) to rewrite the new book and find the best space in the library so that it can stay on an appropriate shelf for a long time and you can access it easily when you need it.

In some disorders, such as Alzheimer's disease, the process of memory consolidation becomes increasingly impaired over time, leading to memory difficulties and, eventually, detriments to an individual's ability to manage self-care and other essential daily tasks. Dr Antonius VanDongen and his team from Duke University seek to understand the roles of specific genes in the complex but critical process of memory consolidation.

The Role of the Arc Gene

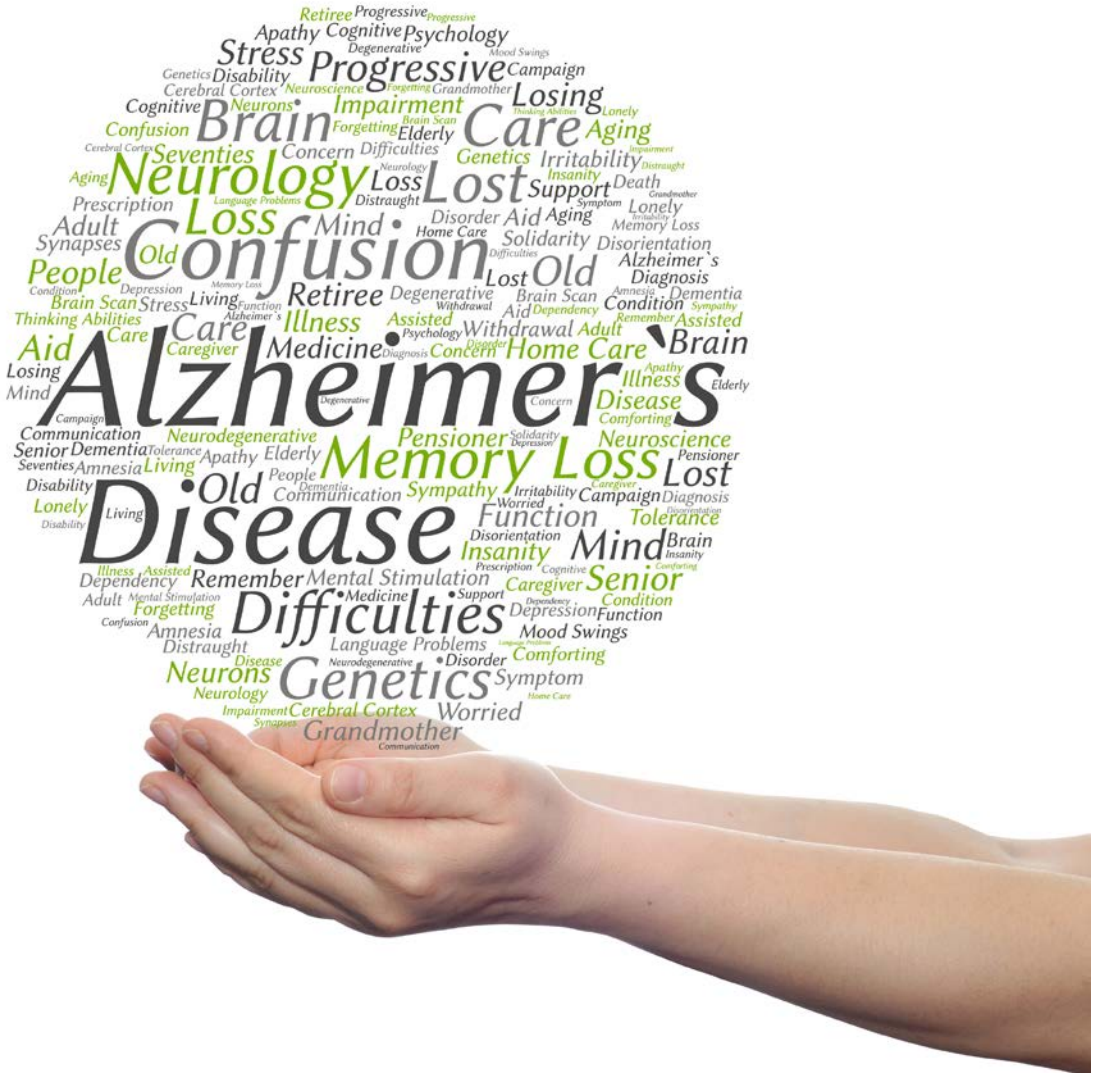
Dr VanDongen is particularly interested in the activity-regulated cytoskeletal-associated protein known as Arc. Deactivation of the Arc gene in mice disrupted long-term memory consolidation, while short-term memory remained unchanged. This means that the Arc gene is involved in specific processes of turning short-term memories into long-term memories, highlighting its importance for memory formation and retention.

Arc acts as a special messenger on synapses, small bridges between our brain cells that allow information to pass from one cell to another. When we learn or experience something new, the Arc gene becomes active and helps our brain to remember and consolidate that experience. As such, it is vital to making our memories solid and long-lasting.

Activating and Deactivating the Arc Gene

Working with How-Wing Leung and Gabriel Wei Quan Foo, Dr Vandongen studied what happens when the Arc gene is deactivated. The (de)activation of a gene and related processes is called gene expression, and the team was able to deactivate the Arc gene in cultured neuronal networks derived from rat brains. Their findings were intriguing.

Disabling the function of Arc altered the gene expression of 1,900 other genes. In other words, altering the expression of the Arc gene directly impacts the function of hundreds of other genes. Some of these genes were related to synaptic functions



or to the functions of other vital brain processes that are involved in memory, learning, and cognition. Significantly, many of these genes are involved in the development of Alzheimer's disease and other forms of dementia. Dr VanDongen's study showed that the Arc gene is essential for consolidating individual memories and is critical to overall brain function. These findings open up a new avenue of research for fully understanding how memories are formed and maintained.

Epigenetic insights into Arc

Recent research revealed fascinating insights into the epigenetic mechanisms that underlie Arc's function. Epigenetics refers to complex modifications of how genes work without altering the genes themselves. So, how does Arc control the activity of other genes?

Dr VanDongen and his colleagues suggest that Arc might affect the 'instructions' that other genes receive. One possible way is to influence the structure of chromatin, a combination of DNA and protein that regulates gene activity. The effect of disabling Arc can be thought of as a series of falling dominoes. Arc's deactivation triggers a cascade of events, starting with changes in chromatin structure. These changes then affect other proteins and molecules, ultimately deactivating multiple genes involved in memory consolidation and synaptic function. This complex interplay is part of the intricate machinery that allows Arc to significantly impact memory and cognitive functions.

Implications for Future Research in Alzheimer's Disease

Due to Arc's role in memory and learning, it offers an important new therapeutic target for slowing down the progression of Alzheimer's disease. By targeting the Arc gene, Dr VanDongen envisions that scientists could potentially develop new therapies for Alzheimer's disease that would work on modulating the gene's activity. Consequently, this would influence the expression of other genes that influence the synaptic functions in neurological disorders, ultimately aiming to address the cognitive dysfunction and memory deficits observed in Alzheimer's disease.

Meet the Researcher

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Dr Antonius VanDongen is an Associate Professor at Duke University, USA. After completing his PhD in Biophysics at the University of Leiden in the Netherlands, he moved to Texas, USA, to work at Baylor College of Medicine. He started working at Duke University in 1992 and at the Duke-NUS Graduate Medical School in Singapore. His extensive background spans pharmacology, electrophysiology, molecular and cellular neurobiology, and computational neuroscience. He is also interested in drug development, and his current research interests include the role of the Arc (activity-regulated cytoskeleton) gene in Alzheimer's disease and the development of related therapeutics.

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FURTHER READING

HW Leung, GWQ Foo, AMJ VanDongen, Arc regulates transcription of genes for plasticity, excitability and Alzheimer's disease, *Biomedicines*, 2022, 10(8), 1946. DOI: https://doi.org/10.3390/biomedicines10081946

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