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Perspective

# Role of Autoimmunity in the Pathogenesis of Alzheimer's Disease

**Robert Harris***

*Department of Immunology, Monash University, Melbourne, Australia*

## DESCRIPTION

Alzheimer's Disease (AD) has been observed to have a higher prevalence in women compared to men, particularly as individuals age. The pathogenesis of AD is complex, involving a variety of inflammatory and autoimmune processes. These processes have been linked to an increased risk of developing AD and research has shown that several autoimmune diseases may contribute to this heightened risk. In general, autoimmune diseases are more prevalent in women than in men, with notable sex differences in the incidence of conditions like multiple sclerosis, rheumatoid arthritis and Sjögren's syndrome. These autoimmune diseases can have significant impacts on brain structure and function, potentially accelerating neural aging. This suggests that women, who are more likely to experience autoimmune conditions, may face an elevated risk for AD, particularly as they age.

While the impact of sex on the prevalence and progression of AD has been well documented, there has been relatively little focus on the specific immunological differences between men and women that might influence brain aging. Recent studies have begun to discover how female-specific immunological processes may affect brain health, particularly during major hormonal transitions such as pregnancy and menopause. These periods are marked by substantial shifts in both hormonal and immune system activity, which may have lasting effects on brain function and aging.

Pregnancy represents a unique phase in a woman's life, during which the immune system undergoes significant changes to accommodate the growing fetus. To avoid rejecting the fetus as a foreign body, the maternal immune system must adapt to a state of tolerance, which involves a delicate balance between pro-inflammatory and anti-inflammatory cytokines. This immune adaptation fluctuates throughout the course of pregnancy, with distinct immunological profiles corresponding to different stages of gestation. Initially, a pro-inflammatory response supports implantation and placentation. This is followed by an anti-inflammatory phase, which facilitates fetal growth and tolerance. Finally, as pregnancy reaches term, a renewed pro-inflammatory response is initiated to trigger labor.

These immune adaptations are not limited to the immune system's interaction with the fetus. The changes in immune function that occur during pregnancy may also influence maternal brain health, particularly by promoting neural plasticity. Neural plasticity refers to the brain's ability to reorganize and form new connections, which is essential for learning, memory and adaptation to new experiences. Pregnancy-related hormonal fluctuations, such as the increase in estrogen and progesterone, have been shown to influence brain structure and function. This can lead to changes in memory, mood and cognition during and after pregnancy. Moreover, studies have suggested that these hormonal changes may have a lasting effect on the trajectory of brain aging, potentially contributing to long-term alterations in cognitive function and the risk of neurodegenerative diseases such as AD.

The immune changes associated with pregnancy are not limited to inflammatory cytokine regulation; they also involve shifts in the maternal microbiome. The microbiome, which refers to the community of microorganisms living in and on the body, plays a critical role in immune function and overall health. External factors, such as infections or disruptions to the microbiome, can affect the immune balance during pregnancy and may have implications for both maternal and fetal health. A well-regulated immune response during pregnancy is essential not only for the successful development of the fetus but also for the long-term health of the mother.

In addition to pregnancy, menopause represents another significant hormonal transition that affects a woman's immune system and brain health. As women transition into menopause, there is a marked decline in the levels of estrogen and progesterone, which can influence a variety of physiological processes, including immune function.

## CONCLUSION

In conclusion, while the link between autoimmune diseases and alzheimer's disease has been established, the role of sex-specific immune processes in brain aging is less well understood. Pregnancy and menopause represent key periods during which women's immune systems undergo significant changes that may influence brain health and aging. Understanding the long-term

**Correspondence to:** Robert Harris, Department of Immunology, Monash University, Melbourne, Australia, E-mail: robert.harris@monash.edu.au

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effects of these immune adaptations could provide valuable insights into the mechanisms underlying sex differences in neurodegenerative diseases and offer new avenues for prevention and treatment strategies tailored to women's unique health needs.