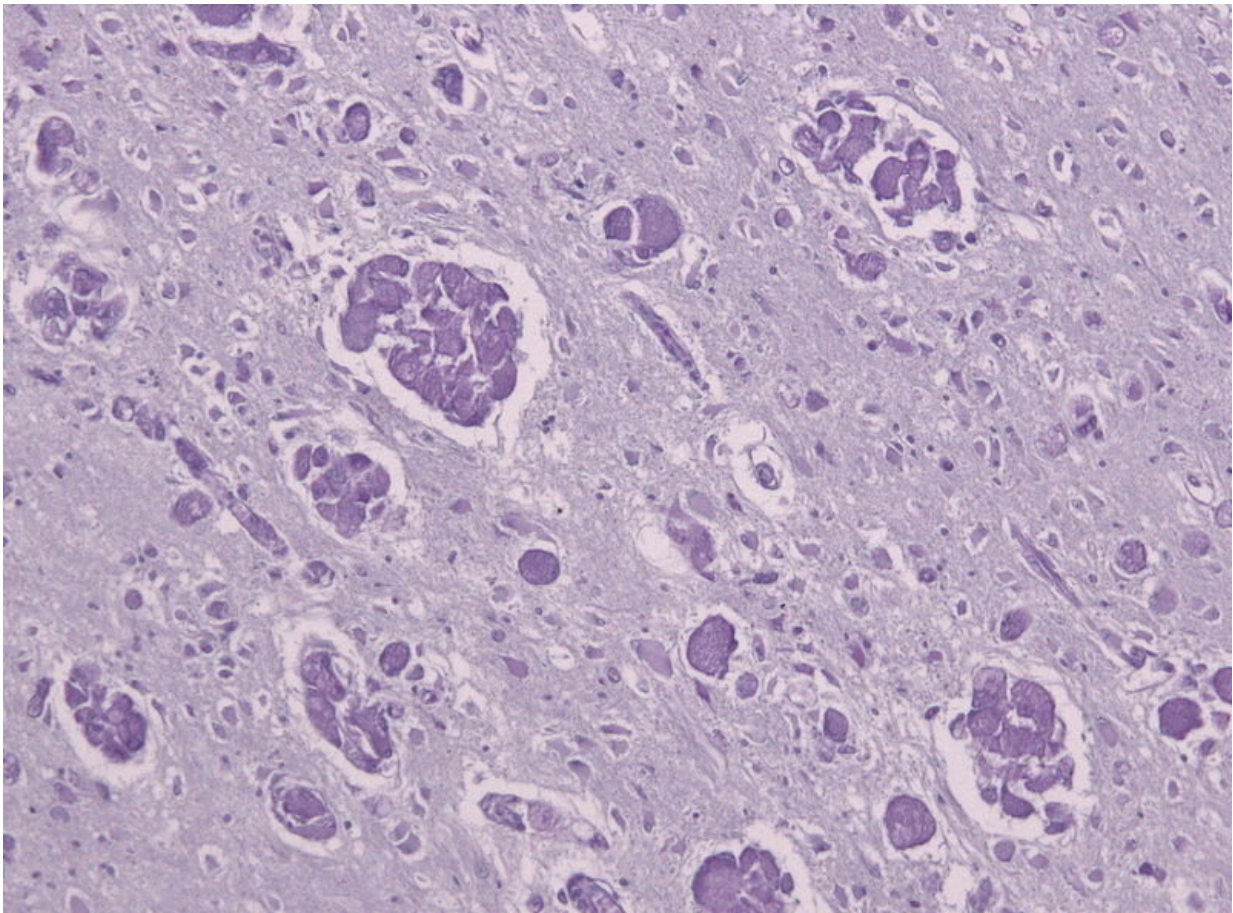


Dementia protein changes discovered in terminal childhood disease

January 10 2022



Mulinucleated macrophages with PAS-positive inclusions ("globoid cells") within astrocytic gliosis and loss of myelinated fibers in a case of Krabbe's leukodystrophy. Credit: [Jensflorian](#)/Wikimedia Commons, CC BY-SA 3.0

In a world-first, researchers at Newcastle University have found that the brains of infants who sadly passed away with an extremely rare genetic condition, Krabbe disease, have similar changes to those seen in two age-related brain diseases, dementia with Lewy bodies and Parkinson's disease. Alzheimer's Research UK funded the research that shows alpha-synuclein has the potential to spread throughout the brain. The scientific journal *Brain* published the findings.

Dementia with Lewy bodies (DLB) and Parkinson's [disease](#) are both [neurodegenerative diseases](#) associated with older age. In both diseases, a protein called alpha-synuclein builds up in the [brain](#) into structures called Lewy bodies, causing damage to nerve cells.

In contrast, Krabbe disease is a rare inherited childhood disorder—with only one case in every 100,000 births. The disease destroys the protective coating surrounding nerve cells in the brain and throughout the nervous system. It is caused by a mutation in the GALC gene, with symptoms showing within the first few months of life. Sadly, the disease typically leads to death in those affected by the age of two.

The team at Newcastle studied post-mortem brain tissue of four infants who died of Krabbe disease. While they did not identify Lewy bodies in the brain tissue of those infants, they did identify changes to the protein alpha-synuclein that are normally associated with DLB and Parkinson's disease.

In particular, the researchers noted that the alpha-synuclein protein in Krabbe disease had the ability to stick together and spread through the brain, a key change associated with dementia with Lewy bodies and Parkinson's disease that is thought to drive the progression of both diseases.

Dr. Daniel Erskine, Alzheimer's Research UK Research Fellow at

Newcastle University, who is an expert in Lewy bodies and led the study, said:

"Looking at the brains of four infants with Krabbe disease compared to four infants without Krabbe disease, we performed a series of experiments to establish the behavior of the alpha-synuclein protein. We found that alpha-synuclein in Krabbe disease shared key qualities that are normally only associated with age-associated neurodegenerative disease like dementia with Lewy bodies.

"This phenomenon has only been reported previously in the brains of older people with neurodegenerative diseases, so seeing it in the brains of these infants is highly remarkable. These findings challenge the view that changes to the brain that underlie these forms of dementia are merely age-associated, but are instead the result of dysfunction of specific biological pathways. This is an important message, as while we cannot stop aging, we can potentially fix something that is not working properly.

"These research findings have only been made possible from the support of the families donating their loved ones' brains for research and I would like to pay tribute to them for their generosity in helping others in a time of unparalleled grief.

"Thankfully, Krabbe disease is a relatively rare condition, however it is devastating for the families affected. Dementia with Lewy bodies affects roughly 100,000 people in the UK. Building on these findings to help develop new drugs that target this common biological pathway could change the lives of people with both conditions."

Dr. Rosa Sancho, head of research at the charity Alzheimer's Research UK, which funded the research, said:

"In dementia with Lewy bodies, the protein alpha-synuclein forms clumps called Lewy bodies inside brain nerve cells. While Lewy bodies were not found in the brains of infants in this study, researchers have shown for the first time that [alpha-synuclein](#) had a similar capacity to spread through the brain in Krabbe disease.

"At Alzheimer's Research UK we often hear dementia dismissed as a normal part of aging. We know dementia is caused by brain diseases, and this research offers more evidence that the disease that cause dementia are caused by biological processes going awry rather than as a by-product of old age.

"Learning about the diseases that cause [dementia](#) from other neurodegenerative conditions and sharing this knowledge with other fields is important. We're incredibly grateful to the families of those whose brains were studied in this research, and who made this important discovery possible."

More information: Christopher Hatton et al, Prion-like α -synuclein pathology in the brain of infants with Krabbe disease, *Brain* (2022).
[DOI: 10.1093/brain/awac002](https://doi.org/10.1093/brain/awac002)

Provided by Alzheimer's Research UK

Citation: Dementia protein changes discovered in terminal childhood disease (2022, January 10) retrieved 3 May 2024 from
<https://medicalxpress.com/news/2022-01-dementia-protein-terminal-childhood-disease.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--