Research sheds light on how proteins linked to Alzheimer's disease influence neuronal growth

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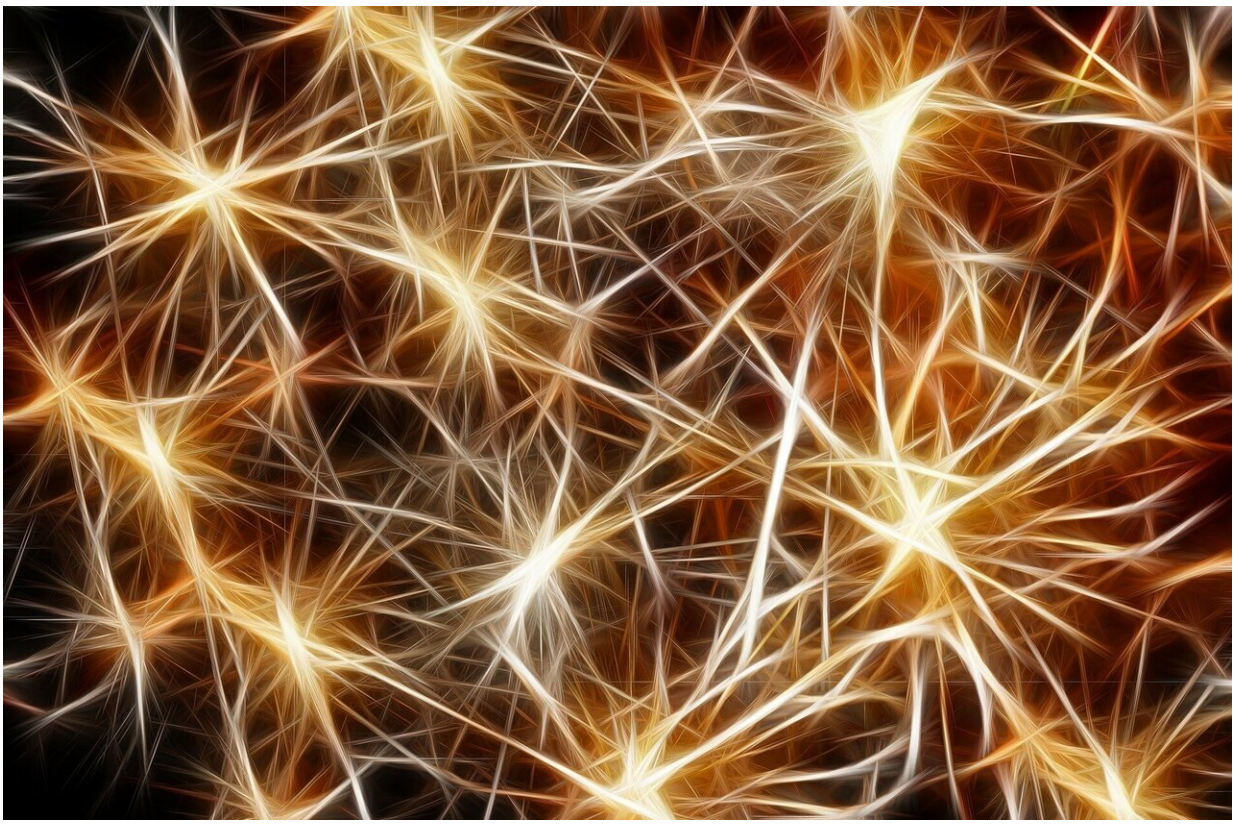

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New research has shed light in the complex interplay between cell proteins, and how they impact on neurons in neurodevelopmental

disorders and Alzheimer's disease.

A new study led by the University of Exeter and published in *Open Biology* has discovered the key role that the protein Contactin-4 (encoded by the gene CNTN4) plays in shaping neurons.

The researchers began studying CNTN4 because it was known to have a role in autism, but its functional roles were not well understood. The team explored how CNTN4 functions within the brain, particularly its interactions with proteins involved in neurodegenerative diseases like Alzheimer's disease.

For the first time, the researchers studied mice who have had the CNTN4 gene knocked out in the cortex, the region of the brain responsible for key functions including memory, thinking and reasoning. They found that neurons developed in a different way in the cortex region.

Researchers have demonstrated for the first time in human cells the interaction between genes CNTN4 and APP, a gene strongly linked to Alzheimer's disease, revealing a co-dependent relationship that is essential for brain development, and specifically for the healthy growth of neurons. They found that CNTN4 not only contributes to neural elongation in the frontal cortex region of the brain, but also CNTN4 expression is regulated via a relationship with APP.

Using studies in genetically modified human cells, the team also discovered that a complex interaction exists between CNTN4 and APP. If CNTN4 is knocked out, then levels of APP decrease, but not to zero. The scientists believe that APP may compensate for the loss of CNTN4, and vice versa.

The study's lead author, Dr. Rosemary Bamford of the University of

Exeter Medical School, said, "It was quite remarkable to discover that CNTN4, a gene linked to developmental processes, also plays a role in modulating factors involved in Alzheimer's disease. This intersection of developmental and neurodegenerative pathways offers exciting new insights into the broader implications of these proteins."

Senior author Dr. Asami Oguro-Ando, of the University of Exeter Medical School, said, "Looking ahead, my group is keen to further dissect the molecular mechanisms underpinning the interaction between CNTN4 and APP and explore their wider implications for disorders like Alzheimer's and autism spectrum disorder. Our next steps involve clarifying how the CNTN4-APP interaction impacts neural activity. Understanding this interaction is crucial as it represents a fundamental step towards a comprehensive grasp of neurodevelopmental and neurodegenerative disorders."

More information: CNTN4 modulates neural elongation through interplay with APP, *Open Biology* (2024). DOI: 10.1098/rsob.240018. royalsocietypublishing.org/doi/10.1098/rsob.240018

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