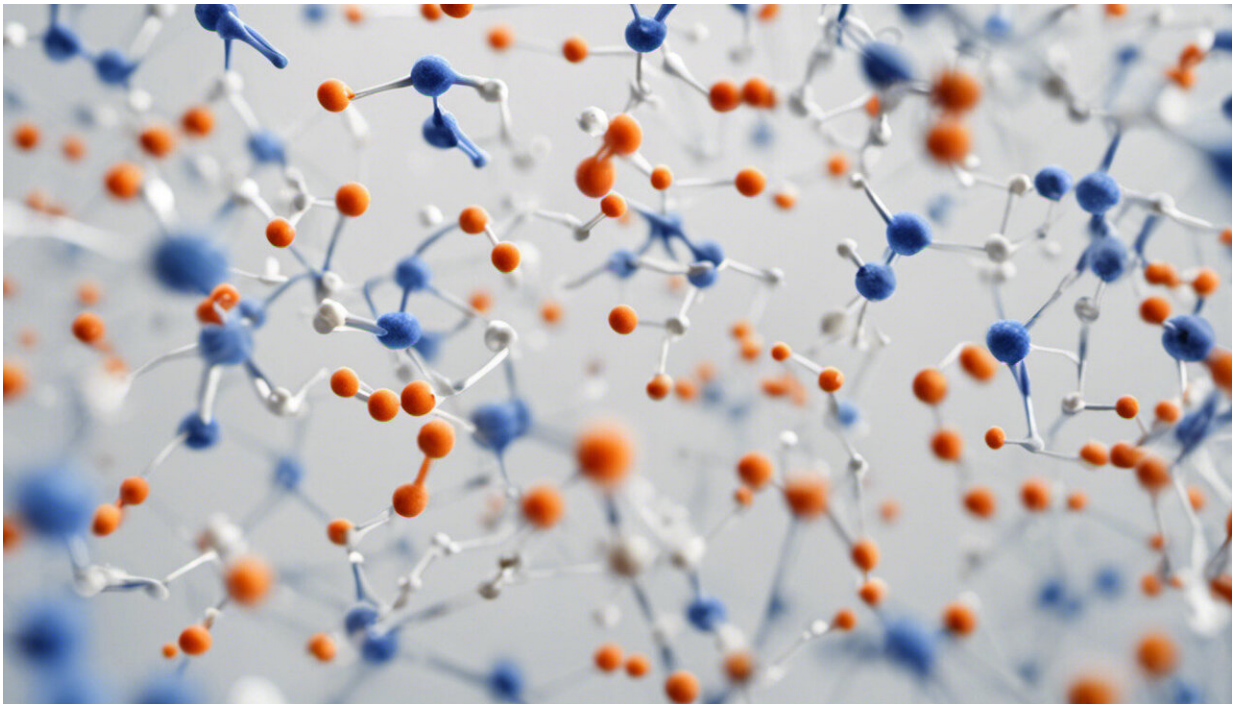


Protein associated with Alzheimer's disease linked to cognitive ability

August 14 2017



Credit: AI-generated image ([disclaimer](#))

If the knowledge that our brains can produce new cells in adulthood is ever going to help in the fight against neurodegenerative disease, we need to understand the underlying mechanisms more effectively. Towards this end, a new study drawing on EU-funded research, sheds further light on the role the protein APP plays in neuroplasticity.

It is known that mutations in the gene responsible for the [amyloid precursor protein](#) (APP) are implicated in the development of Alzheimer's Disease (AD). However, a new study recently published in the *Journal of Alzheimer's Disease*, and drawing on work from the EU-funded AGGRESSOTYPE project, has reported for the first time a link between these protein variants and childhood cognitive ability.

The study specifically observed an association between the APP gene and Performance IQ (PIQ). PIQ is believed to reflect fluid intelligence, referring to problem solving and reasoning abilities reliant on working memory, unlike so-called crystallised intelligence which denotes accumulated knowledge. The work raises questions about the protein's role in neuroplasticity and later cognitive disorders.

The role of neuroplasticity in cognitive health

Communication between cells in the brain occurs via synapses which contain specialist proteins. Intellectual and cognitive function relies on this neural network retaining adaptability, known as neuroplasticity. However, mutations in some of these synaptic proteins can lead to brain dysfunctions and disorders, such as epilepsy or autism.

Researchers in this study focused specifically on a cluster of genes referred to collectively as the 'ARC complex' for their association with the Activity-regulated cytoskeleton associated protein (Arc). Arc and its regulators and inter-actors are known to facilitate neuroplasticity. However, the genes in the ARC complex have also been implicated in a number of conditions characterised by cognitive disabilities, most notably, Alzheimer's' Disease. The study was therefore predicated on the theory that the ARC complex may be an important determinant of cognitive abilities throughout the lifespan and also of age-related dementia.

To conduct the study, the researchers analysed both the IQ scores and genetic markers of 5,165 children from the Avon Longitudinal Study of Parents and Children. They then examined the DNA sequence variations of 17,008 adults with AD, alongside 37,154 healthy adults. They also considered the genetic data of 112,151 adults assessed on cognitive functions.

Tracking the pathways from molecules to behaviour

The study indeed found that a variation in the DNA sequence within the gene encoding the APP protein was associated with children's fluid intelligence. In adults, this same variation has been associated with AD. Additionally, the genetic variation within the APP gene appeared to be correlated with the efficiency of information processing (expressed as reaction time). It is known that APP encodes a [protein](#) that forms creates neuritic plaques or extracellular deposits in the grey matter of the brain, considered to be a pathological hallmark in AD brains. However, it is not known how these plaques affect brain functions and whether they themselves lead to AD.

The research team have described their work as 'exploratory' and called for follow-up studies to more accurately understand how APP variations may affect cognitive function over a lifetime. It is hoped that this increased etiological understanding will eventually lead to treatment for cognitive dysfunctional disorders, such as AD.

The AGGRESSOTYPE (Aggression subtyping for improved insight and treatment innovation in psychiatric disorders) project which enabled some of the study's work, was set up to explore the biological basis of aggression, focusing specifically on childhood disorders, such as [attention-deficit hyperactivity disorder](#) (ADHD). It takes a multidimensional approach, which includes inputs from genetics, brain

imaging and epigenetics, as well as cognitive and behavioural assessments.

The project aims to develop algorithms for aggression prediction, accompanied by treatment options including not only pharmacological but also non-pharmacological strategies, such as biofeedback. It is estimated that aggressive psychiatric disorders affect more than 5 million children or adolescents in the EU and cost the health system more than six billion Euros per year to manage.

More information: Project website: www.aggressotype.eu/

Provided by CORDIS

Citation: Protein associated with Alzheimer's disease linked to cognitive ability (2017, August 14) retrieved 10 April 2024 from <https://medicalxpress.com/news/2017-08-protein-alzheimer-disease-linked-cognitive.html>

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