# Article information:

Alzheimer's disease is associated with reduced expression of energy metabolism genes in posterior cingulate neurons | PNAS
<https://www.pnas.org/doi/full/10.1073/pnas.0709259105>

# Article summary:

1. Alzheimer's disease is associated with reductions in the expression of nuclear genes encoding subunits of the mitochondrial electron transport chain (ETC) in metabolically affected brain regions, particularly the posterior cingulate cortex.

2. The reduction in neuronal expression of these metabolically relevant nuclear genes may be associated with cerebral metabolic rate for glucose abnormalities found in FDG PET studies of AD.

3. These findings suggest potential targets for disease-slowing and prevention therapies for AD.

# Article rating:

May be slightly imbalanced: The article presents the information in a generally reliable way, but there are minor points of consideration that could be explored further or claims that are not fully backed by appropriate evidence. Some perspectives may also be omitted, and you are encouraged to use the research topics section to explore the topic further.

# Article analysis:

The article "Alzheimer's disease is associated with reduced expression of energy metabolism genes in posterior cingulate neurons" published in PNAS presents a study that aimed to investigate the molecular basis of Alzheimer's disease (AD) by comparing the expression of metabolically relevant nuclear genes from laser-capture microdissected non-tangle-bearing neurons of expired cases with clinically characterized and histopathologically verified AD and expired controls who did meet clinical criteria for dementia and histopathological criteria for AD. The authors found that AD cases had significantly lower expression of 70% of the nuclear genes encoding subunits of the mitochondrial electron transport chain in posterior cingulate cortex, which is metabolically affected in the earliest stages, compared to controls.

The study provides valuable insights into the pathogenesis of AD and new targets at which to aim disease-slowing and prevention therapies. However, there are some potential biases and limitations that need to be considered. Firstly, the sample size was relatively small, with only 10 AD cases and 10 controls included in the study. This may limit the generalizability of the findings. Secondly, it is unclear whether other factors such as age or comorbidities could have influenced gene expression levels. Thirdly, while the study focused on metabolically relevant nuclear genes from laser-capture microdissected non-tangle-bearing neurons, it did not investigate other cell types or regions that may also contribute to AD pathogenesis.

Another potential limitation is that the study only investigated gene expression levels and did not examine protein levels or functional changes in mitochondria. While Western blots confirmed underexpression of those complex I–V subunits assessed at the protein level, further studies are needed to confirm whether these changes affect mitochondrial function.

Additionally, while the study provides evidence for a link between reduced neuronal expression of nuclear genes encoding subunits of the mitochondrial electron transport chain and CMRgl reductions found in FDG PET studies of AD, it does not explore other possible mechanisms underlying these reductions.

Overall, this study provides important insights into the molecular basis of AD but further research is needed to confirm these findings and explore other potential mechanisms underlying CMRgl reductions found in FDG PET studies of AD.

# Topics for further research:

* Mechanisms underlying CMRgl reductions in Alzheimer's disease
* Mitochondrial dysfunction in Alzheimer's disease
* Role of age and comorbidities in gene expression levels in Alzheimer's disease
* Other cell types and regions involved in Alzheimer's disease pathogenesis
* Functional changes in mitochondria in Alzheimer's disease
* Disease-slowing and prevention therapies for Alzheimer's disease

# Report location:

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