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Ground-breaking Alzheimer's findings reveal new treatment strategy

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(PhysOrg.com) -- Alzheimer's disease affects the major two types of brain cells, neurones and neuroglia. For a long time glial cells have been thought to have a purely supportive role. However, recent work and more specifically ongoing studies at the University of Manchester are probing a much more relevant functional role including new treatment opportunities, for neurodegenerative processes such as Alzheimer's disease.

Dr José J. Rodríguez Arellano and Professor Alexei Verkhratsky believe that, contrary to popular belief, neuroglial cells (astrocytes) in the brain shrink during Alzheimer's disease. Astrocytes are vital in providing for generation and maintenance of synapses and therefore diminished astroglial support alters synaptic connectivity thus redusing brain cognitive power. They say that probably the new strategies aimed at protection and support of neuroglia may help to combat brain degeneration in Alzheimer disease.

Dr Rodriguez-Arellano, whose work was funded by the Alzheimer's Research Trust, says: "These are amazing findings and totally unexpected. We have found that model animals (transgenic mice) with Alzheimer's pathology have problems with glial cells as well as with the neurones in the brain.

"Everybody thought that glial cells grew bigger in response to the disease but we have found that some of them actually shrink and this causes serious problems. Glial cells are not merely supportive; they have an

active role in maintaining synapses so the imbalance of these cells can have a serious negative effect."

The team's novel research, published in the Nature group journal Cell Death and Differentiation, shows that whilst glial cells grow bigger around the protein plaques caused by Alzheimer's disease (AD), probably to protect nerve cells near the affected area, those further away shrink. This stops the glial cells providing an effective support for synaptic connections, which in parallel to the loss of neurones can be one of the major the causes of brain damage in AD.

The team, based at Manchester's Faculty of Life Sciences, now plans to combine these findings with those from two other studies, on the effects of AD on the production of new neurones (neurogenesis), to design a treatment to be given at the first sign of AD.

They have found that AD reduces neurogenesis in both the hippocampus and subventricular zone. In both areas, the reduction in neurogenesis was directly associated with the presence of AD protein plaques and an increase in the number of neurones containing this protein. The studies, published in the journals PLoS ONE and Neuroreport, showed that disrupted neurogenesis occurred at a much younger age in females, correlating with the higher prevalence of AD in women.

Rebecca Wood, Chief Executive of the Alzheimer's Research Trust says: "This research is making fantastic progress. By understanding what is happening in the brain during Alzheimer's, we can arm ourselves with the tools to develop new treatments. The brain is hugely complex, and this new research shows how Alzheimer's can affect not just nerve cells but also other cell types.

"We desperately need to support research that can move us towards new treatments. With the population living with dementia forecast to double

within a generation, we are in a race against time."

Dr Rodríguez Arellano says: "It is conceivable that a recovery in neurogenesis rates in AD could help rescue cognitive impairment.

"We believe both restoring and/or increasing the rate of neurogenesis as well as designing a glial support treatment in the early stages of AD will halt its progression, possibly even reverse the process."

The team (PhD students Harun Noristani, Markel Olabarria Larizgoitia and Chia-Yu Yeh) is now seeking further funding so they can test the use of growth factors on glial cells and explore a range of treatments to increase neurogenesis.

Citation:

• 'Astroglia in dementia and Alzheimer's disease' in Cell Death and Differentiation.
• 'Impaired Adult Neurogenesis in the Dentate Gyrus of a Triple Transgenic Mouse Model of Alzheimer's' in PLoS ONE.
• 'Impaired Cell Proliferation in the Sub-Ventricular Zone in an Alzheimer Disease Model' in Neuroreport.

Source: The University of Manchester