Examining the effects of S1P receptor drugs in Alzheimer’s disease

https://www.neurodegenerationresearch.eu/survey/examining-the-effects-of-s1p-receptor-drugs-in-alzheimer%c2%92s-disease/

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Ireland

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Research Abstract
Alzheimer’s disease (AD) is set to affect 1 in every 3 people as the global demographics age. To date, however, treatments against AD are limited and if left untreated AD will likely have unmanageable implications on healthcare, financial and societal systems. Sphingosine 1-phosphate receptors (S1PRs) are composed of subtypes S1PR1-5 and are expressed on many cells types including those of the immune, cardiovascular and central nervous systems. S1PRs are targets for the drug fingolimod, which is the first oral therapy recently approved for use in patients with multiple sclerosis (MS). The phosphorylated version of fingolimod (pFTY720) binds to all S1PRs, except S1PR2. Studies have shown pFTY720 internalises S1P1Rs on T cells

limiting their egress from lymph nodes and limiting inflammatory response in MS. Importantly, pFTY720 also binds to S1PRs on neuronal and glial cells and is thought regulate neuronal and glial cell survival, proliferation, differentiation, migration and function. Recently, the S1PR modulator fingolimod (pFTY720) has been shown to be beneficial in animal models of AD. We hypothesise that the protective effects of pFTY720 in animal models of AD are likely mediated through its effects on both immune and neuronal/glial cells, with the S1PR1 and S1PR5 subtypes playing a major role. Given that pFTY720 is a pan-S1PR modulator, here we aim to demonstrate if selective S1PR1 and S1PR5 compounds mediate protective effects in animal models of AD. This work will (i) corroborate previous findings for use of S1PR drugs in AD and (ii) clarify the S1PR profile required for a drug to be use in AD. Both these findings will be pivotal in designing and implementing a clinical trial that tests the use of S1PR drugs in AD.

Further information available at:

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