MACABSTRACTS

EFFECT OF NEUROFIBRILLARY TANGLES ON BEHAVIOURAL FLEXIBILITY IN RATS: ANIMAL MODELS FOR FRONTO-TEMPORAL DEMENTIA AND ALZHEIMER'S DISEASE

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Neurofibrillary tangles (NFTs) are aggregations of abnormal tau protein implicated in neurodegenerative diseases such as behavioural-variant frontotemporal dementia (bvFTD) and Alzheimer's disease (AD), dementias that exhibit a large degree of symptom overlap. NFTs are prominent in the prefrontal and entorhinal cortices in early-stage bvFTD and AD, respectively. We modeled this site-specific neurodegeneration in rats via microinjection of a viral vector to express an excess of mutated tau protein in these target areas. We then examined the impact of this somatic gene transfer on performance in the following behavioural flexibility task. The rats were initially trained to find food rewards in a plus maze using a place strategy: to always go to the same place in the environment, i.e., north or south. Subsequently, they switched to a response strategy: to always make the same body response, i.e., turn right or left. Rats made a total of six switches between place and response strategies, and their acquisition and retention of each switch was measured and compared to controls. We found that bvFTD model rats could acquire the place strategy, but were impaired when acquiring the response strategy. AD model rats were impaired in acquiring both strategies. For both groups, there were no impairments in retention of either strategy. Together, these findings suggest patterns of performance on a behavioural flexibility paradigm can differentiate between animal models of early bvFTD and AD. Future research can use these findings to screen novel candidate drugs, and study mechanisms underlying AD and bvFTD.

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HUMAN ENTERIC GLIAL CELLS ALLEVIATE DAMAGED ADULT SENSORY NEURONS IN RATS

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Spinal cord injury affects millions across the globe, and its prevalence is rising with the increasing rate of accidents. Not much is known regarding the cellular mechanism of injury, and, unfortunately, there are few viable treatment options. One option may be transplantation of peripheral nerves into the site of injury, but the peripheral nervous system is not readily accessible, and doing so could disrupt the functioning of other areas. One part of the nervous system, however, is accessible: the enteric system, embedded in the lining of the gastrointestinal tract. This system bears similarities to the central nervous system, has remarkable plasticity, and releases growth factors, which not only facilitate regeneration of neurons, but also protect the enteric nervous system from damage. Previous research shows rat enteric glial cells induce regeneration in rodent neurons *in vivo* with a crushed spinal cord and *in vitro* to dorsal root ganglia treated with semaphorin-3A to mimic spinal cord injury. We study whether human enteric glia bear similar effects *in vitro* on rodent dorsal root ganglia. Our experiments to date show this treatment is viable, emphasizing its use in clinical trials. It proves to be a particularly successful transplantation technique since the donor cells originate from the host, thereby minimizing the chance of rejection.

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COMPOUND 186 IS A NEGATIVE ALLOSTERIC MODULATOR OF DOPAMINE D2 RECEPTORS: IMPLICATIONS FOR IMPROVING SCHIZOPHRENIA THERAPY

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Excessive dopamine transmission in the striatum via the dopamine D2 receptor (D2R) has been implicated in inducing the so-called positive symptoms of schizophrenia (e.g., hallucinations, delusions). While antipsychotic drugs alleviate these symptoms by blocking the active site of this receptor, drugs known as allosteric modulators could also decrease dopamine's ability to bind this receptor by binding to an allosteric site on D2R. We evaluated the ability of a newly synthesized molecule, compound 186, to modulate the binding of tritiated norpropylapomorphine (NPA)–a high-affinity D2R agonist–in the bovine striatum. Through receptor binding assays, we found a significant decrease in NPA binding with compound 186, in a dose-dependent manner. Our study suggests a potential method to treat dopaminergic disorders such as schizophrenia. Because many current treatments for schizophrenia block the active site of D2R elicit severe side effects, such as tardive dyskinesia and diabetes, it is important to consider changing the therapeutic approach from using antagonists to allosteric modulators.

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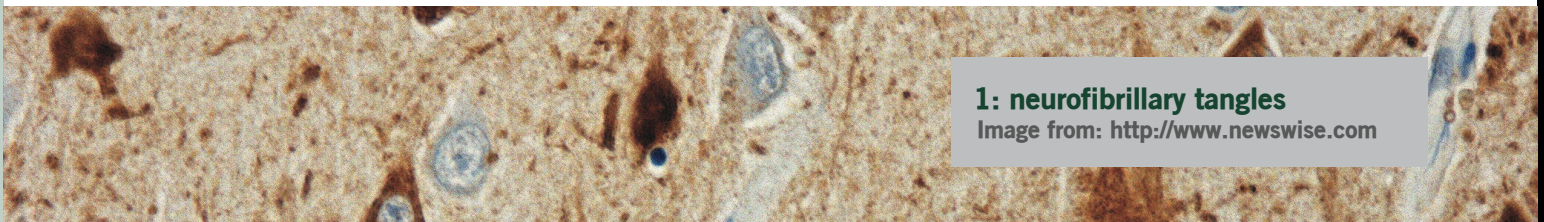

1: neurofibrillary tangles
Image from: http://www.newswise.com