INTRODUCTION

Alzheimer’s disease (AD) is characterized by progressive memory loss and impairments in language and behaviour. The cognitive decline is accompanied by neuronal atrophy and loss, mainly in the cortex, hippocampus, and amygdala. Neurofibrillary tangles in AD are extracellular senile plaques, deposits of amyloid β, and intraneuronal aggregates of paired helical filaments (PHFs), composed of hyperphosphorylated forms of the microtubule-associated protein tau. GSK3β is a serine/threonine protein kinase that is particularly abundant in the CNS. GSK3β is known to participate in multiple signalling pathways, and has been postulated to be a key player in tau hyperphosphorylation and β-amyloid-induced neurotoxicity and neurodegeneration. The contribution of GSK3β to the pathogenesis of AD and the role of its inhibitors are still under investigation.

TgGSK3β MICE OVEREXPRESS GSK3β IN THE CORTEX AND HIPPOCAMPUS

NOVEL OBJECT RECOGNITION BEHAVIOURAL TEST

The novel object recognition test (NOR) assesses the ability to recognize a novel object in a well-known environment. The test was performed in a cage with two identical objects. A novel object was introduced and the time spent exploring the novel object was recorded. Animals were considered to have recognized the object when the animal spent more than 5 min close to the novel object.

MORRIS WATER MAZE BEHAVIOURAL TEST

The Morris water maze (MWM) task involves placing the rat in a pool of water where it must use visual cues to remember the location of a hidden platform just beneath the water’s surface. The MWM test measures spatial learning and memory. This test is one of the most popular tasks in behaviour neuroscience and is sensitive to both the amyloid and memory-enhancing effects of drugs as well as gene manipulation dependent on intact hippocampal function.

The parameters measured were time to reach the platform (s), distance swam (m), speed (m/s), latency time to each quadrant, and number of times crossing the entry platform.

AGE AND LEARNING CAPACITY IN THE OBJECT RECOGNITION TEST

The animals were subjected to the Object Recognition Test. Eight 12-week-old mice and twelve 24 and 30-week-old mice were tested. The memory index (M) was calculated using the formula: M = (t1 + t2) / (t1 + t2 + t3), where t1 represents the time exploring the novel object, t2 the time exploring the old object, and t3 the time exploring the new object. The M value was calculated for each mouse. In all age groups, wild-type mice showed higher recognition than experimental groups.

AGE AND LEARNING CAPACITY IN THE MORRIS WATER MAZE

The animals were subjected to Morris water maze test. Eight 12-week-old mice were tested and twelve 24 and 30-week-old mice were tested. The MWM test measures spatial learning and memory. This test is one of the most popular tasks in behaviour neuroscience and is sensitive to both the amyloid and memory-enhancing effects of drugs as well as gene manipulation dependent on intact hippocampal function.

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CONCLUSION

Conditional TgGSK3β double transgenic mice show GSK3β overexpression in the brain, leading to increased tau phosphorylation levels and reactive gliosis. We have determined their performance at different ages in two standard learning and memory paradigms such as the Morris water maze and the novel object recognition test. When compared to wild-type TgGSK3β transgenic mice, the result showed a unique animal model for AD and an invaluable tool for testing the therapeutic potential of selective GSK3β inhibitors.