INTRODUCTION

The presenilin 1 (PS1) C311F mouse model of Alzheimer’s disease (AD) is useful for the study of AD-related phenomena. The PS1 (C311F) mouse model shares some AD-related behavioral deficits with human AD patients, including learning and memory impairments, increased oxidative stress, and increased amyloid-ß (Aß) levels. The PS1 (C311F) mouse model also develops cortical atrophy, muscle weakness, and shortened lifespan. Aß is an amyloidbeta protein and is a major pathological hallmark of AD. Aß accumulates in senile plaques, which are characteristic of the AD brain. Aß is produced by the proteolytic cleavage of the amyloid-β precursor protein (APP) by ß-secretase and ß-secretase-like enzymes. Aß is toxic to neurons and induces oxidative stress, reactive oxygen species (ROS) generation, and inflammation. The central nervous system is rich in ß-secretase activity, and the genetic complement of ß-secretase is highly conserved. ß-secretase activity is enhanced in the aging brain, which suggests that ß-secretase is associated with the pathogenesis of AD.

Aß can be found in the brain extracellular matrix, where it interacts with several proteins and enzymes. Aß can also be found in the blood plasma, where it can be detected using specific antibodies. The presence of Aß in the extracellular matrix is associated with the deposition of Aß plaques and neurofibrillary tangles, which are characteristic features of AD. The presence of Aß in the blood plasma is associated with the presence of Aß plaques in the brain.

Aß can also be found in the cerebrospinal fluid (CSF), where it can be detected using specific antibodies. The presence of Aß in the CSF is associated with the presence of Aß plaques in the brain.

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Materials and methods

Animals

Male C57BL/6 mice (8 weeks old) were purchased from Harlan (Barcelona, Spain) and housed in a temperature-controlled room (22 ± 2°C), with a 12:12 h light:dark cycle (lights on at 07:00). Mice were housed in groups of 4-5 per cage and provided with food and water ad libitum. Mice were randomly assigned to the different experimental groups. At the beginning of the experiment, mice were weighed and their body weight was recorded. Mice were allowed to acclimate to the experimental environment for at least 1 week before the start of the experiment. Mice were divided into four groups: control (C), ANAVEX2-73 (1 mg/kg), donepezil (0.1 mg/kg), and memantine (0.3 mg/kg). The dose of donepezil was based on the pharmacological profile of donepezil in the literature. The dose of memantine was based on the pharmacological profile of memantine in the literature. The dose of ANAVEX2-73 was based on the pharmacological profile of ANAVEX2-73 in the literature.

Drug treatments

Mice were injected intraperitoneally (i.p.) with saline (C), ANAVEX2-73 (1 mg/kg), donepezil (0.1 mg/kg), and memantine (0.3 mg/kg) daily for 7 days. Mice were injected once a day between day -7 and day -1 before disease induction. Mice were injected once a day at 0.1 mg/kg donepezil and 0.3 mg/kg memantine, respectively. ANAVEX2-73 was injected at 0.1 mg/kg, 0.3 mg/kg, and 1 mg/kg.

Behavioral tests

Spatial navigation was assessed using the Morris water maze. The Morris water maze is a two-dimensional water maze with a hidden platform. Mice were required to swim to a hidden platform to escape from the water. The platform was located at the center of the maze, and the time taken by each mouse to reach the platform was recorded. The Morris water maze is a useful tool for the assessment of spatial navigation and memory.

Memory consolidation was assessed using the Y-maze, which is a one-dimensional maze with a hidden platform. Mice were required to swim to the hidden platform to escape from the water. The time taken by each mouse to reach the platform was recorded. The Y-maze is a useful tool for the assessment of memory consolidation.

Locomotor activity was assessed using the open-field test, which is a one-dimensional maze with a hidden platform. Mice were required to swim to the hidden platform to escape from the water. The distance travelled by each mouse was recorded. The open-field test is a useful tool for the assessment of locomotor activity.

Oxidative stress was assessed using the malondialdehyde (MDA) assay, which is a sensitive measure of lipid peroxidation. MDA is a product of lipid peroxidation and is a sensitive measure of oxidative stress. The MDA assay was performed according to the manufacturer’s instructions.

Enzyme activities were assessed using specific methods. Cholinesterase activity was assessed using the colorimetric method of Chevion et al. (1974). AChE activity was assessed using the spectrophotometric method of Ellman et al. (1961). GABAergic activity was assessed using the spectrophotometric method of Bilkey et al. (1973). Glutamatergic activity was assessed using the spectrophotometric method of Chen et al. (1986).

Histopathological analysis was performed using standard methods. Tissue samples were fixed in formalin, embedded in paraffin, and sectioned. The tissue sections were stained with hematoxylin and eosin (H&E) and examined by light microscopy.

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REFERENCES


