

“Reduction of neuroinflammation and cognitive impairment induced by A β on a yarrow model type APP/PS1 having as a target protein kinase 2 activated by MAPK”

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Scientific Report

Summary

Alzheimer's disease (AD) is a form of dementia with no current treatment. The pathological hallmark of AD is the deposition of amyloid- β (A β) that cause disruption in synapse communication mainly in brain areas associated with cognitive dysfunction is associated with impairment of a form of synaptic plasticity in the hippocampal area of the brain. We have recently showed that manipulating the MAP kinase-activated protein kinase 2 (MK2) protein we can rescue the impairment in synaptic plasticity and cognitive impairment in the APP/PS1 animal model of AD.

Aim of the study

Here we aim to test the hypothesis that using an inhibitor of MK2 is sufficient to delay/prevent cognition dysfunction in AD mice at 7 months of age.

Objectives to be delivered in the first 6 months of the project

1. Project implementation. Setting up the behavioral facility and purchase of the APP/PS1 colony of mice.

2. Obtain the ethical approval to perform the experimental work..

3. Breeding and ageing of the animals required to perform the experimental work.

During the first 6 months, major preparations have been made as outlined in the first components of work package 1 (WP1)-as described below and following the outline of the project objectives:

1. All the members of the project team have now been hired and together they form a strong group that will enable success of the project within the given time frame
2. As described in WP-1 (months 1-12), acquisitions were made to obtain the equipment and software needed to conduct the project. So we have now set up and optimised the Barnes Maze (used to assess cognitive/memory changes), the imaging system for monitoring, and the new software (Any-Maze see Figure 1 below) that assesses behavioural changes activity and movement.



Figure-1

The Barnes maze is ready for use see figure-2 below-



Figure-2

3. The mice (APP/PS1-were obtained from the Kackson Laboratories in USA; and MK2 have arrived and bedded in) are in the process of being crossed in order to generate the novel APP/PS1XMK2 knockout. As described in WP 1.1- Four genotypes are being reared those being tested will be APP/PS1XMK2 knockout versus APP/PS1, versus MK@ knockout, versus wild-type controls-see Figure 3 below:



Figure-2 (details of the maze table optional regions of exploration)

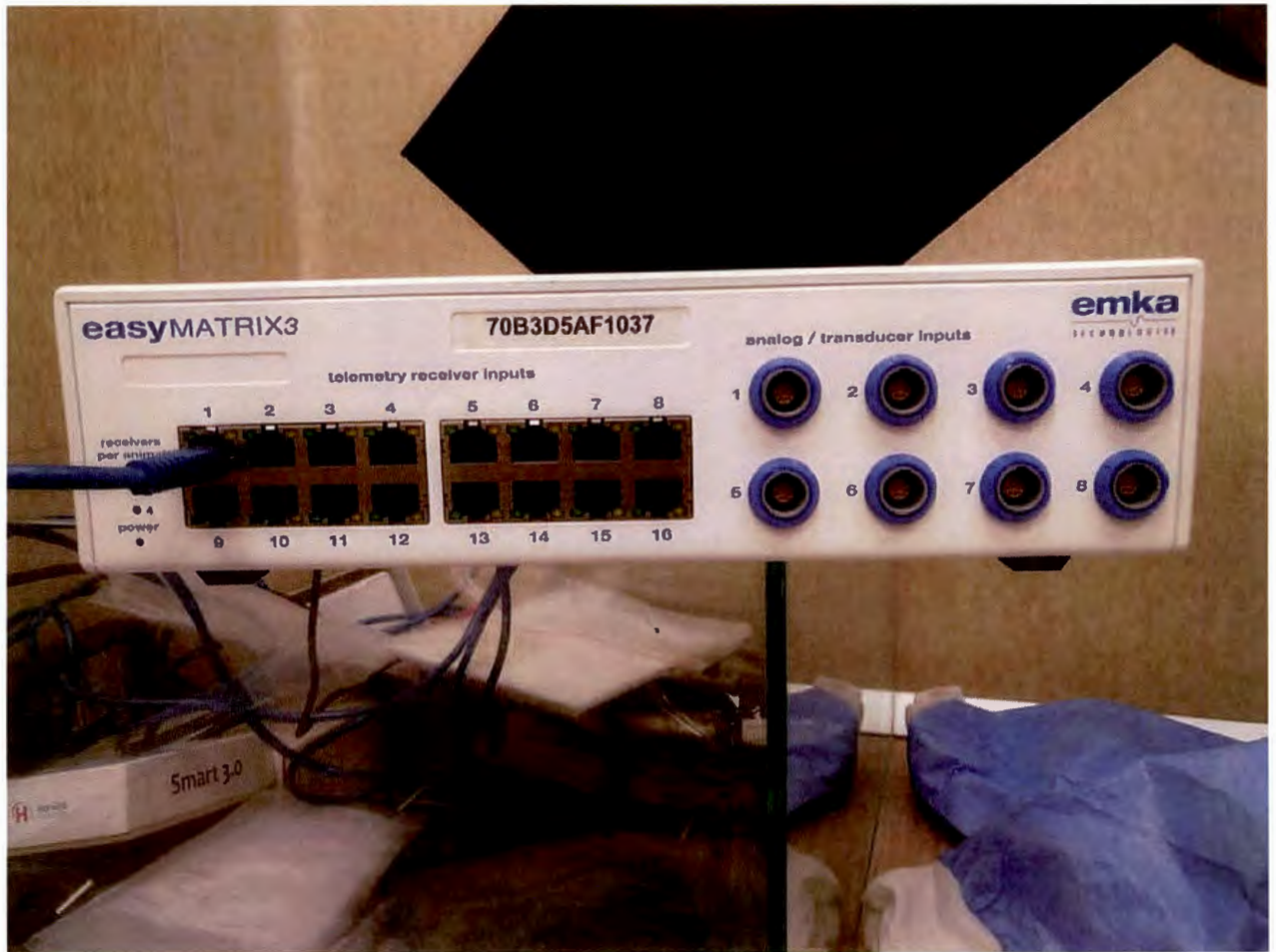


Figure-2 electronic set up



Figure-3 The new mice strains in quarantine and ready for mating



Figure-3 mouse breeding set up

All mice are currently, All mice will be housed under identical conditions in individually ventilated cages on standardized rodent bedding (Rettenmaier®, Germany) in the Association for Assessment and Accreditation of Laboratory Animal Care-accredited animal facility of UMFST, Romania. Cotton nestlets (Plexx®, The Netherlands) will be provided as nesting material. The room temperature is kept at approximately 21 °C, and the relative humidity, between

40% and 70%. Mice are being housed under a constant light-dark cycle (12 hours light/dark).

Over the next 6 months:

The crossed mice will have bred to the numbers required and stage WP1.2 will be initiated when they reach 7 months of age in March. Spatial learning differences will be monitored in single and double knockout mice versus wild-type with details as described in the project. We are on schedule.

In relation to the objectives:

The first tangible objective has been completed here-that is preparation of the animal facility, acquisitions of equipment software materials mice models and computer and novel software this is finalised

Also the team is fully recruited and ready to operate during the next phase in January.

The next objective is to determine the effects of the MK2 deletion in the APP/PS1 mice and see if cognitive impairment is blocked, this work will be completed between January 2023-end June 2023 (months 7-12 of the project).

Project manager

Prof.univ.dr. Mark Anthony Slevin

A handwritten signature in blue ink, reading "M. A. Slevin", with a long, sweeping horizontal line extending to the right.