Mouse Spatial Recognition Test
Testing Hippocampal Function in Alzheimer's Disease Model

SynAging uses proprietary amyloid-β oligomer (AβO) preparations to induce Alzheimer's disease in mice.

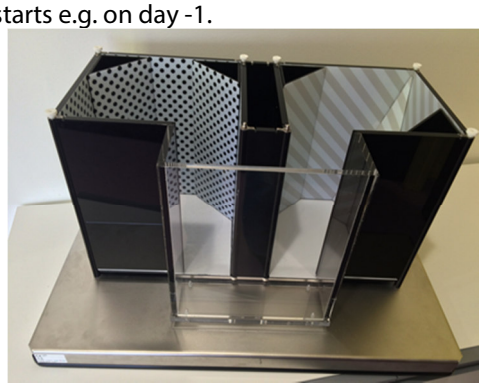
SynAging's AβO preparations induce cognitive deficiency within days which remain stable over multiple months. SynAging has verified the cognitive deficiency of AβO injected mice in the following assay formats:

- Y-Maze (pre-frontal cortex)
- Novel Object Recognition (perirhinal cortex)
- Morris Water Maze (hippocampus)

Topographical memory (TM) is the ability to recall the contours, design, shape, or structure, and is linked to hippocampal function (Ref.1). TM is disrupted during the early stages of Alzheimer's disease (Ref. 2). The spatial recognition test (SRT) is sensitive to donepezil and memantine (Ref. 3), drugs used for Alzheimer's disease treatment.

SynAging validated the disruption of TM in the SRT by amyloid-β oligomers (AbO). In comparison to the well established Morris Water-Maze, SRT is also hippocampus-dependent, but does not involve a learning component, making it **fast and cost effective and allowing longitudinal studies.**

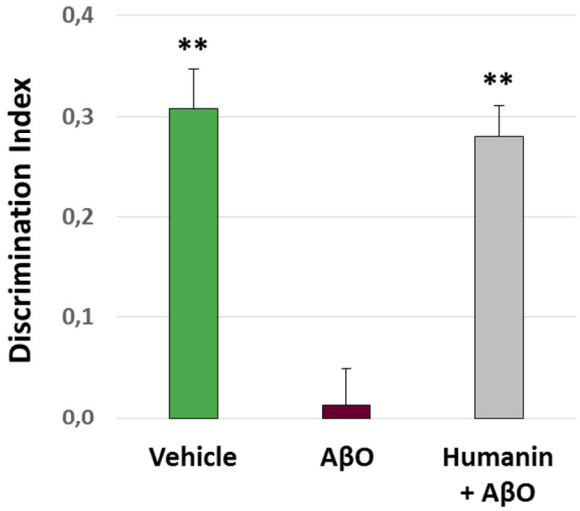
Evaluation of test compound mediated improvement of hippocampal function is performed in the SRT assay: mice are injected icv with vehicle or AβO (day 0), while test compound treatment starts e.g. on day -1.



SRT uses a two-chamber apparatus, in which both chambers differ in shape, pattern and colour (i.e. are topographically different). The two compartments are connected by a clear Plexiglas corridor. No habituation is necessary.

The initial 5 min. 'sample' phase allows only the exploration of one chamber. Following a 30-min interval in the home cage, mice are placed back in the apparatus for a 5-min 'choice' phase, in which they can explore both chambers.

The active exploration time in the novel chamber is compared to that in the familiar chamber and the discrimination index is calculated: DI = (TN − TF)/(TN + TF), in which TN is the time investigating the novel chamber, and TF is the time investigating the familiar chamber.



**, different from AβO (p<0,01)

In the figure above, the results are presented (day 15):
Vehicle-injected control mice can differentiate between familiar and novel chamber, whereas AβO-injected mice do not differentiate, as they lost the memory of the familiar chamber. Humanin, co-injected with AβO, can rescue the AβO-induced cognitive decline.

The SRT assay can be repeated after 14 day intervals in longitudinal studies so e.g. with and without acute compound dosing, to evaluate disease modifying effects.

References:

Ref. 1: Hartley et al.,2007 Hippocampus, 17(1):34-48
Iaria et al.. Hippocampus. 2014; 24(11): 1364-74
Hartley T, Harlow R. 2012, Front Hum Neurosci. 201; 6: 338
Ref. 2: Bird et al., 2010; Hippocampus.; 20(10): 1154-69
Pengas et al., 2010; J Alzheimers Dis. 2010; 21(4): 1347-65
Ref 3: Godley et al., 2015, J Psychopharmacology. BAP poster

SynAging SAS
2 Rue du Doyen Roubault
Vandoeuvre-les-Nancy
54518, France

President:
Violette Koziel
CEO/CSO:
Thierry Pillot

Contact for Europe & USA:
Dr. Andreas Köpke
andreas.kopke@synaging.com
Tel : +49 6136 957 3000

SIRET N°: 520 189 838 00029
VAT N°: FR61520189838