# Cognitive Assessment of transgenic mice with Alzheimers Disease

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## Purpose

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by the accumulation of beta-amyloid (Aβ) plaques in the brain, leading to cognitive decline and behavioral changes. While current diagnostic methods rely heavily on brain imaging and cognitive assessments, earlier detection of AD remains a significant challenge. Recent studies have suggested that Aβ accumulation may also occur in the eye, specifically in the retina and lens, potentially offering a non-invasive and accessible diagnostic pathway.

Raman spectroscopy has emerged as a promising technique for detecting Aβ deposits in ocular tissues, providing a detailed molecular fingerprint based on the vibrational energy shifts of scattered photons. This technique offers high sensitivity and the ability to detect Aβ buildup in both in vivo and ex vivo tissue samples. By analyzing retinal and lenticular tissues in transgenic AD mice, Raman spectroscopy could serve as a powerful tool for early detection of AD, allowing for a better understanding of the role of eye-based biomarkers in the disease's progression.

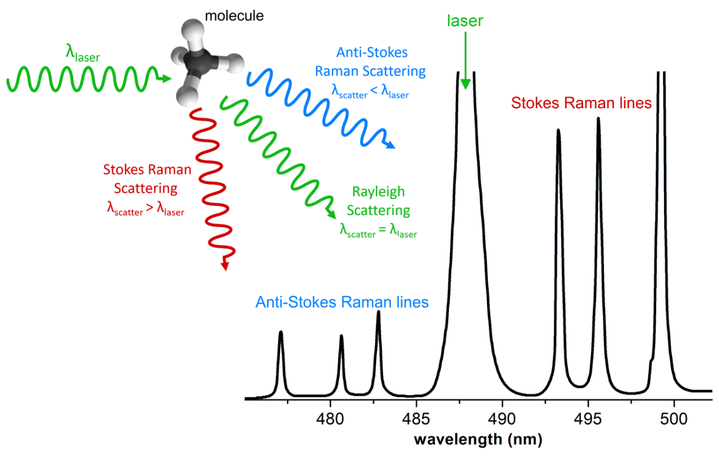
The presence of biomarkers characteristic for Alzheimer's disease in the retina is a controversial topic. Utilizing chemometric modeling, Steibing et. al detected subtle biochemical alterations in AD mice. Sharifzadeh et al. demonstrated that healthy human retinas can be examined in vivo using Raman spectroscopic imaging (RSI), revealing the distribution of macular pigments and paving the way for potential early diagnosis of retinal diseases.

In this study, we aim to evaluate the use of Raman spectroscopy in detecting Aβ accumulation in the retina and lens of AD mice. By combining this with behavioral assessments and genetic validation, we hope to explore the potential for Raman spectroscopy as an early diagnostic tool for Alzheimer's disease.

## Methods

To examine the relationship between cognitive, behavioral, and structural changes in AD, we utilized a range of tests in transgenic 5xFAD AD mice and wild-type (WT) mice at multiple time points (6, 9, and 12 months). These test include:

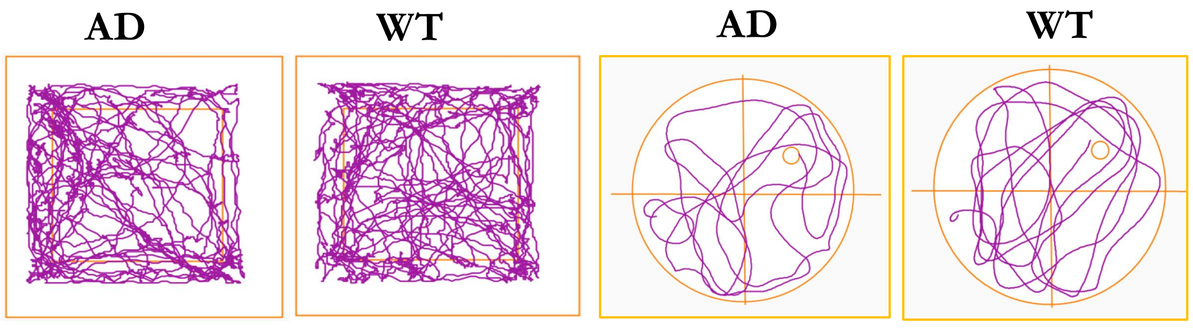
| *Tears collection* | *Morris water maze* | *Open field test* | *Raman Spectroscopy* |
|---|---|---|---|




**Raman spectroscopy:** The laser focuses on the sample, causing a small portion of scattered photons to lose energy, which is absorbed by the molecule's vibrational energy levels. By using a spectrometer to measure the shifted photons (with altered wavelengths after filtering out the original laser light), we can obtain a spectral fingerprint of the molecules, with intensity reflecting their density.

## Results

**1. Morris water maze and open field test did not prove locomotor activity or anxiety related behavior change between young AD and WT mice**

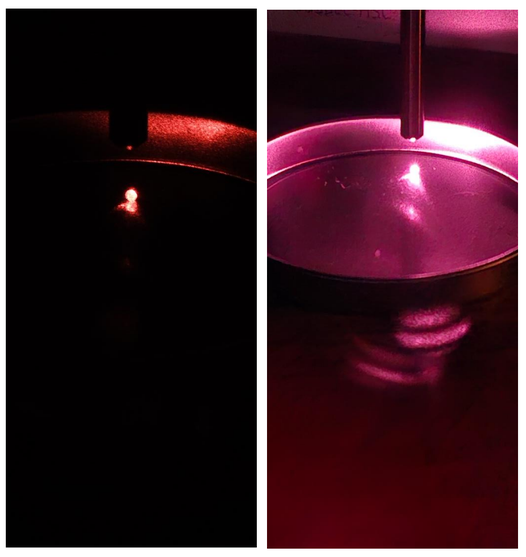



**Open field test:**
- **Time immobile**
- **Freezing episodes**
- **Freezing time**

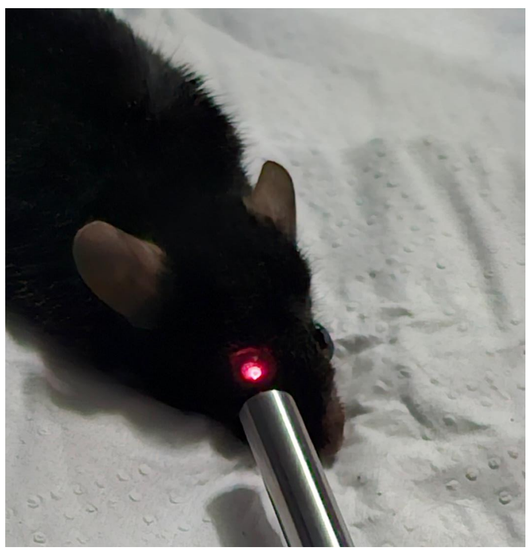
**Morris water maze:**
- **Escape latency time**
- **Distance traveled**

## Results - continued

***Ex-vivo***

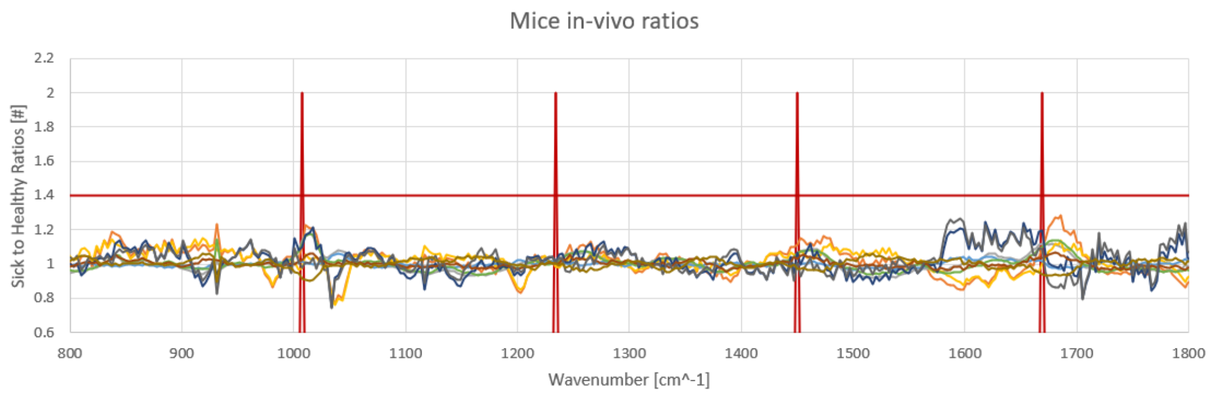


***In-vivo***

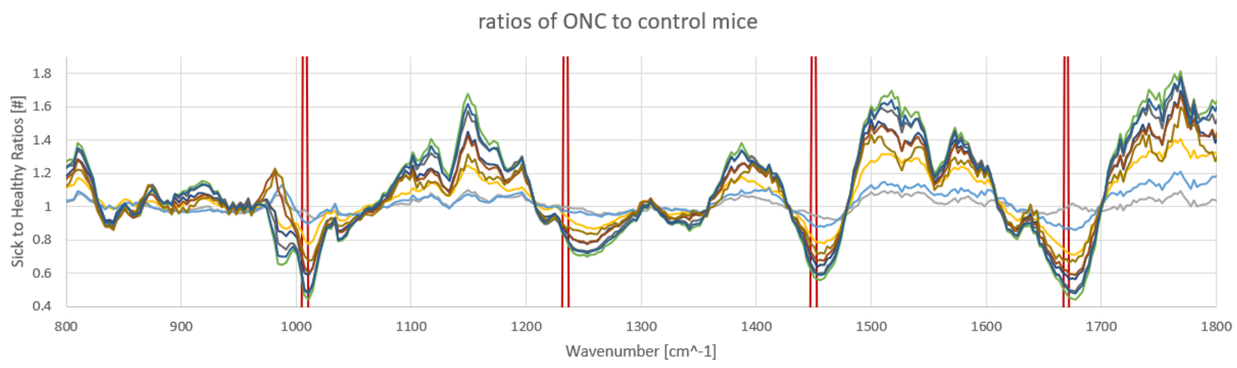


**Aβ accumulation detection:** Raman spectroscopy was applied to an *ex-vivo* mouse lens and *in vivo* mouse retina, ear, and tail tissues to assess beta-amyloid (Aβ) accumulation. This technique enabled the detection of Aβ deposits by analyzing the energy shifts of scattered photons, providing insight into Aβ buildup in different tissues.

**2. *In-vivo* Raman spectroscopy imaging was performed on the lenses of 8 months old control mice**




**3. *Ex-vivo* Raman spectroscopy showed difference in Aβ fingerprint in lens of optic nerve crush mice compared to WT control**




## Conclusions

**Ongoing Research in Alzheimer's Disease Mouse Models**

1. Preliminary ex vivo and in vivo analyses in mice
2. Initial behavioral studies comparing young AD mice to controls

**Future Research Directions**

- Longitudinal in vivo Raman spectroscopy imaging of AD mice vs. controls
- Comprehensive ex vivo analysis of mouse lenses and retinas using Raman spectroscopy, compared with multimodal imaging techniques
- Extended behavioral studies contrasting AD and wild-type mice

**Multimodal Imaging Techniques**

- PET-CT with flutemetamol
- Manganese-enhanced MRI

## Acknowledgment

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**References**:

1. Xu et al. Accuracy of Raman spectroscopy in the diagnosis of Alzheimer's disease, Front. Psychiatry, 2023
2. Harnessing the power of Raman spectroscopic imaging for ophthalmology. Li et al. Front. Chem., 2023