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Novel Insights into Cartenoid Association with Amyloid Aggregates in Brain Tissue

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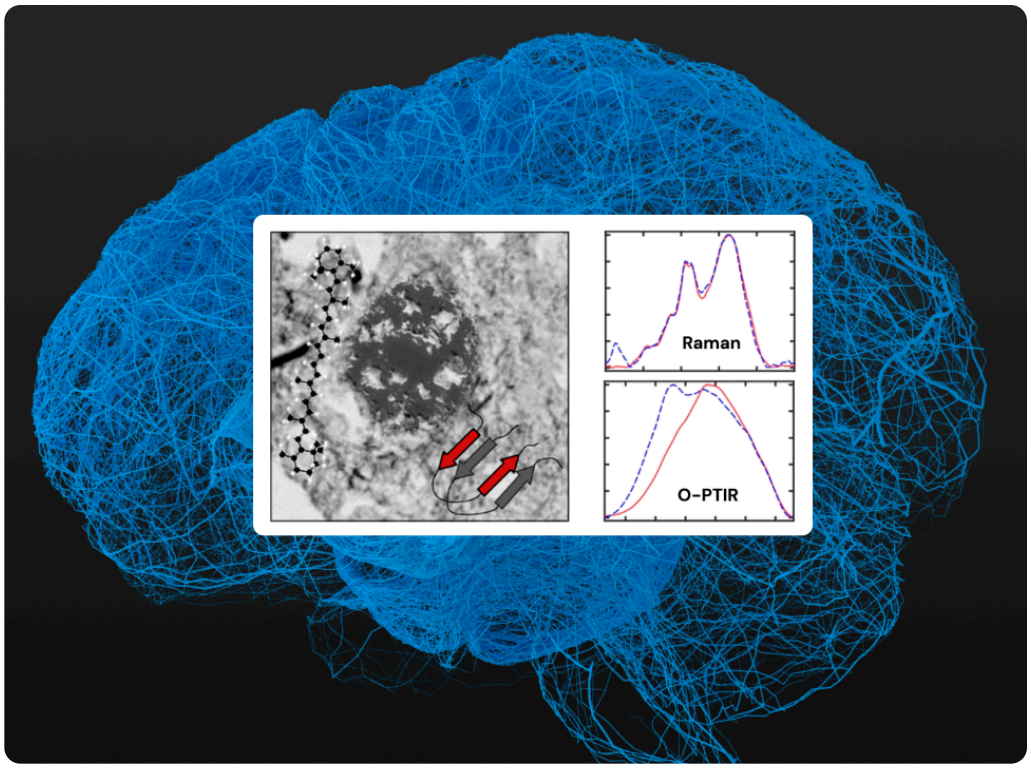
| Webinar brief (https://www.photothermal.com/webinar-brief/)



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This article is based on a webinar hosted by Photothermal Spectroscopy Corp, featuring insights from Assoc. Prof. Ayanjeet Ghosh, Dept of Chemistry and Biochemistry, University of Alabama.

Amyloid aggregates in the brain are primarily associated with two major diseases: Alzheimer's disease (AD) and cerebral amyloid angiopathy (CAA). In AD, these aggregates form amyloid plaques in the brain parenchyma, while in CAA, they accumulate in blood vessels. Despite extensive research, both conditions lack definitive diagnosis methods and effective treatments, with an estimated 70-80% of Alzheimer's patients also showing features of CAA.

Structural Analysis Challenges

While the structure of amyloid fibrils has been well-studied in vitro, understanding their composition and structure within brain tissue presents significant challenges. Traditional biophysical techniques such as NMR, cryo-EM, and conventional IR spectroscopy lack the spatial resolution needed to study individual aggregates in tissue samples. This limitation has hindered our understanding of:

- The composition of specific amyloid aggregates
- Chemical entities associated with amyloid beta
- Variations between different plaques within the same patient
- Changes across different disease stages

Novel Spectroscopic Approach

To address these challenges, researchers employed a combination of two complementary techniques:

- Mid-infrared photothermal microscopy (O-PTIR)
- Raman spectroscopy
- This combined approach offers several advantages:
- Sub-micron spatial resolution (~500 nm)
- Capability to study samples in their native tissue environment
- Complementary chemical information from both techniques
- Ability to analyze both protein structure and associated compounds

Key Findings

Cartenoid Association

- Approximately 18% of analyzed amyloid plaques contained cartenoids
- Cartenoids were found in roughly 40% of examined cortical blood vessels
- The presence of cartenoids strongly correlates with higher beta-sheet content

Structural Insights

Two distinct types of amyloid aggregates were identified:

- Cartenoid-containing aggregates with high beta-sheet content
- Cartenoid-depleted aggregates with lower beta-sheet content

IR spectroscopy revealed:

- Increased intensity around 1630 cm-1 in cartenoid-containing plaques

- Clear correlation between beta-sheet content and cartenoid presence
- Slight increase in lipid content in cartenoid-associated aggregates

Mechanistic Implications

The research suggests two possible mechanisms for cartenoid association:

Anti-inflammatory response:

- Cartenoids may be recruited to address neuroinflammation
- This appears more likely based on experimental evidence

Disaggregation mechanism:

- Cartenoids might act as disaggregating agents
- However, experiments with beta-carotene treatment showed minimal changes in beta-sheet content

Methodological Innovation

The study demonstrates the power of combining Raman and O-PTIR microscopy for correlative microscopy.

- Raman spectroscopy excels at detecting and identifying cartenoids
- O-PTIR provides detailed information about protein secondary structure
  The combination offers comprehensive chemical characterization of amyloid aggregates

Significance and Future Directions

This research reveals previously unknown chemical associations in amyloid aggregates and suggests that certain types of plaques may be more relevant to neurodegeneration and neuroinflammation. The findings open new avenues for understanding:

- The role of cartenoids in neurodegenerative diseases
- The relationship between plaque structure and inflammation
- Potential therapeutic targets based on plaque composition

The study also establishes a powerful new methodology for analyzing complex biological structures in tissue samples, combining the strengths of multiple spectroscopic techniques. This research was conducted at the University of Alabama's Department of Chemistry and Biochemistry, with support from the National Institutes of Health and collaboration with neuropathologists at Duke University.

For more detailed information watch the webinar:
Alzheimer's Disease Research with Sub-micron Simultaneous IR+Raman
(https://www.photothermal.com/webinars/alzheimers-disease-research-with-sub-micron-simultaneous-irraman-co-localization-of-beta-sheets-and-carotenoids-in-aggregates/)

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