

Spectris™ Sensory Stimulation Increases CSF HDL-Like Lipid Transport Proteins in Alzheimer's Disease

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Background

Cholesterol and lipid-transport dysfunction contribute to Alzheimer's disease (AD) pathophysiology. It has been observed that CSF APOA1 was lower in AD and associated with both MMSE and CSF pTau181¹. Preclinical evidence suggests that increasing APOA1 expression may improve cognition, reduce neuroinflammation, and support synaptic and myelin integrity²⁻⁴. We describe the effect of investigational Spectris™ treatment on CSF lipid transport proteins.

Methods

We conducted CSF proteomics in amyloid-positive MCI participants (n=10) enrolled in the FLICKER trial (NCT03543878)⁵. Participants used the investigational Spectris sensory stimulation device daily for 1 hour for either 8 (N=5) or 4 (N=5) weeks (delayed start design). CSF was collected at baseline, 4 weeks, and 8 weeks; proteins were measured by using mass tagged peptides in unbiased tandem mass spectrometry⁶. Changes in protein abundance were compared between participants who received 8 weeks treatment (n=5) and participants (n=5) who did not receive stimulation; proteins were mapped to published brain protein co-expression modules⁷ via Go Elite (version 1.2.5) to assess the impact of Spectris treatment on AD-related pathophysiological pathways⁸.

References

1. Johansson P et al. *J Alzheimers Dis.* 2017.
2. Button EB et al. *Acta Neuropathol.* 2019.
3. Lewis TL et al. *J Neurosci.* 2010.
4. Lui H et al. *Mol Ther.* 2020.
5. He Q et al. *Alzheimers Dement.* 2021.
6. Zhou M et al. *Clin Proteomics.* 2020.
7. Johnson ECB et al. *Nat Neurosci.* 2022.
8. Hajós M et al. *Alzheimers Dement.* 2025.

Results

- Spectris treatment induced consistent up-regulation of CSF lipid transport proteins, including APOA1, APOA2, and APOL1—key components of HDL-like lipid transport or metabolism (Figure 1).
- GO Elite pathway analysis demonstrated that 13/29 upregulated pathways (red) involve lipid transport or metabolism (Figure 2).

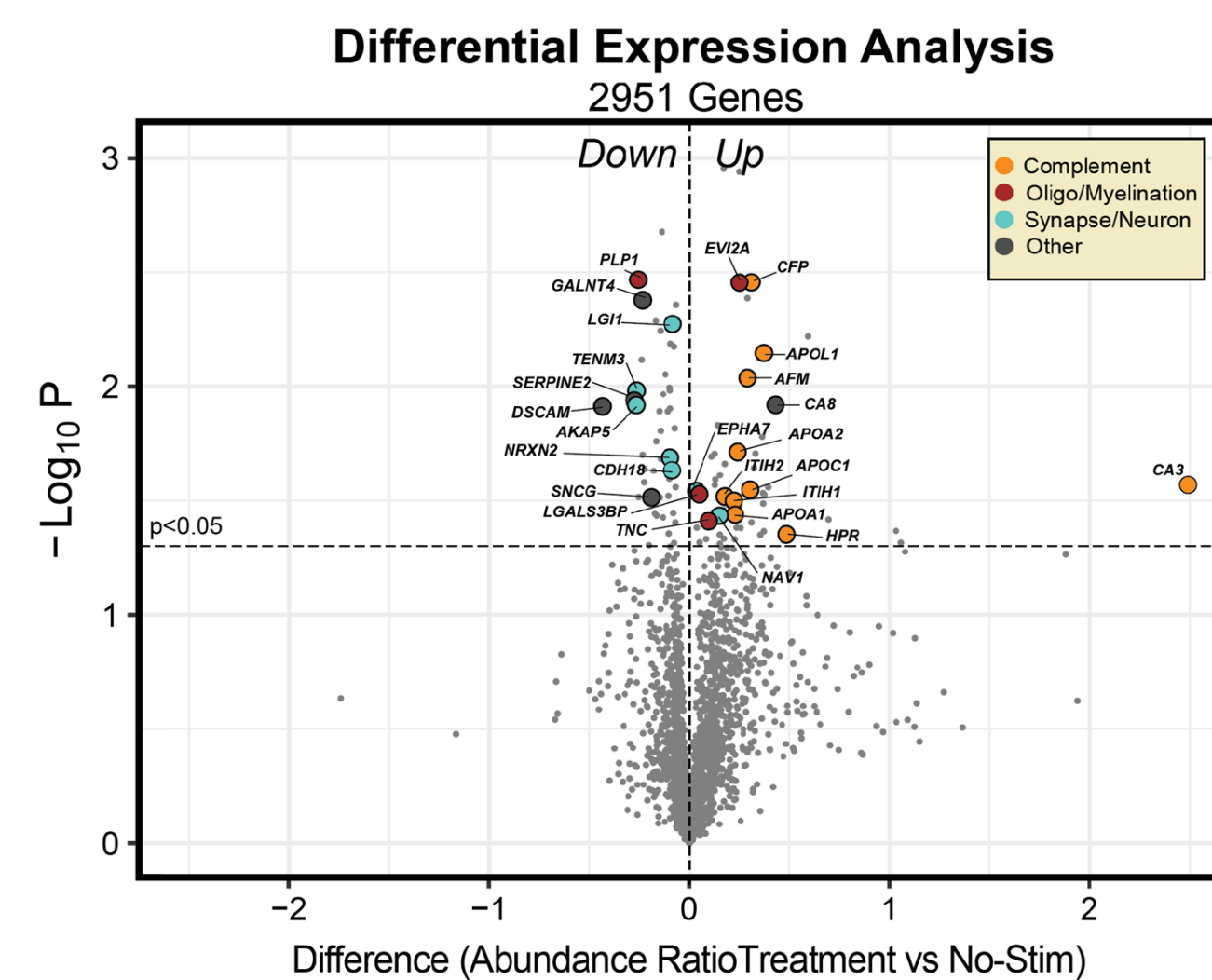


Figure 1. Unbiased CSF proteomics volcano plot showing up-regulated lipid-transport proteins following Spectris™ treatment (from Hajós et al., 2025, *Alzheimer's & Dementia*)⁸.

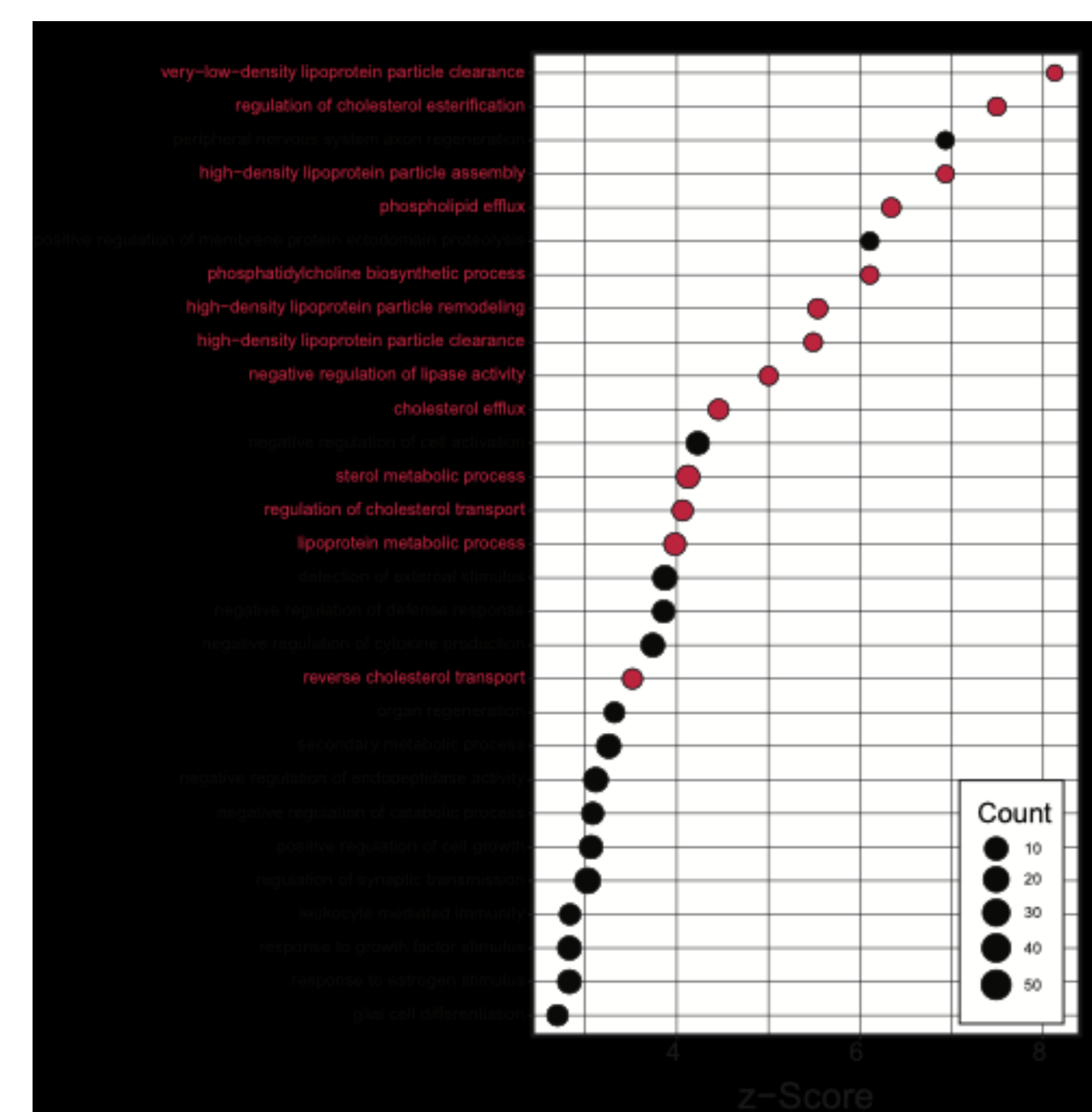


Figure 2. Pathway-enrichment map highlighting up-regulated lipid-transport pathways (red) following Spectris™ treatment (from Hajós et al., 2025, *Alzheimer's & Dementia*)⁸.

Conclusions

- Spectris treatment increased CSF levels of lipid transport proteins in the treatment group.
- Enhanced CSF lipid-transport protein levels may support myelin maintenance, synaptic repair, and immune regulation.
- These preliminary biomarker findings support further investigation of HDL-like lipid transport proteins as a potential brain resilience pathway and as a potential biomarker in future AD clinical trials.