

Circulating Extracellular Vesicles and Physical Stress in ME/CFS

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Research Group Website: <https://neuroimmune.cornell.edu/research/vesicles-and-signaling/>

Primary CNF Tools Used: Malvern NS300 NanoSight

Abstract:

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a debilitating and complex multisystem illness that affects millions in the United States. Individuals with ME/CFS suffer from persistent fatigue, cognitive impairment, unrefreshing sleep, and post-exertional malaise (PEM), a worsening of symptoms following physical or mental exertion. Growing evidence suggests that extracellular vesicles (EVs), membrane-bound particles released by all cells, play a role in mediating intercellular communication and may contribute to disease pathology. In this project, we used the Malvern NanoSight NS300 Nanoparticle Tracking Analysis (NTA) system to measure concentration of plasma-derived EVs from ME/CFS patients and matched controls across multiple time points surrounding a cardiopulmonary exercise test (CPET). Accurate quantification of EVs is essential not only to assess physiological responses to exercise but also to normalize downstream EV cargo analyses, including surface protein profiling using flow cytometry and RNA-based studies.

Summary of Research:

We used the Malvern NS300 NanoSight NTA instrument to characterize EV populations in plasma samples collected from 28 individuals with ME/CFS and 26 healthy controls. Blood samples were taken before, shortly after, and 24 hours following a CPET. EVs were isolated using standardized protocols to ensure consistency across samples.

Nanoparticle tracking analysis was performed to determine the concentration of EVs in each sample. The resulting data (Figure 1) demonstrate that there is no significant difference in baseline EV concentrations between ME/CFS patients and healthy controls. However, a significant increase in EV concentration was observed in both groups shortly after CPET. This

was followed by a marked decrease in EV levels during the recovery phase (24 hours post-exercise), suggesting dynamic regulation of EV release in response to physical exertion in both healthy and diseased states.

Quantification data from the NTA are also being used to normalize EV input for multiplex surface marker profiling using flow cytometry kits and for RNA cargo analysis. This normalization step is crucial for ensuring meaningful biological comparisons across subjects and time points.

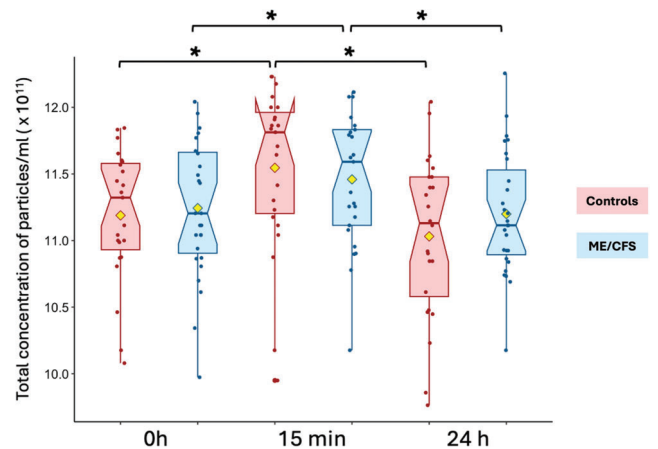


Figure 1: Characterization of extracellular vesicles by Nanoparticle Tracking Analysis. Total concentration of particles per mL of plasma across three time points: before exercise (0h), 15 minutes post-exercise, and 24 hours post-exercise.

Conclusions and Future Steps:

Our findings reinforce that EV concentrations increase after exercise and subsequently decline during recovery in both ME/CFS and control groups. This exercise-responsive EV dynamic highlights the utility of NTA for identifying physiologically relevant changes and enabling normalization across sample sets. Ongoing studies are expanding the dataset with additional subjects to improve statistical power. Future work will

focus on integrating surface protein signatures from immunophenotyping using flow cytometry and RNA cargo analysis, allowing us to correlate EV content with exercise response and clinical severity in ME/CFS. These efforts aim to uncover biomarkers of PEM and dysfunctional intercellular signaling in ME/CFS, ultimately improving our understanding of disease mechanisms and therapeutic targets.

References:

- [1] Giloteaux Ludovic and Maureen R. Hanson. Post-exercise changes in mitochondrial DNA of extracellular vesicles in myalgic encephalomyelitis/chronic fatigue syndrome. Poster presentation by L. Giloteaux at the International Society of Extracellular Vesicles (ISEV) 2025 conference held in Vienna, Austria, April 23rd-27th.