Circulating Extracellular Vesicles and Physical Stress in ME/CF

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Primary CNF Tools Used: Malvern NS300 Nanosight

Abstract:

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a chronic, complex, multisystemic condition characterized by long-term fatigue that does not improve with rest, persists for more than six months, and other associated symptoms, and cannot be explained by any other underlying medical condition. The cause of ME/CFS remains unknown, and no established diagnostic tests, nor universally effective treatment are available.

Introduction:

A hallmark of ME/CFS is a distinctive Post-Exertional Malaise (PEM), which occurs following physical or cognitive exertion and can last from days to weeks. Research on the physiological responses to exercise in ME/CFS subjects supports disruptions and disturbances in the central nervous system, cardiovascular and immune system with impaired muscular energy metabolism. Following exercise challenge, skeletal muscle can impact the whole body physiology through secretion of diverse biomolecules into exosomes (exersomes) such as muscle-derived humoral factors (myokines) and exercise-induced humoral factors (exerkines) in a regulated and targeted manner.

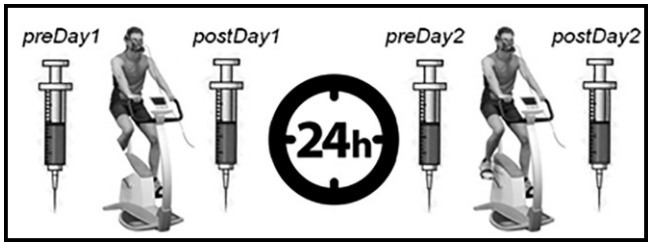

Figure 1: ME/CFS patients and age-and gender-matched sedentary controls will perform two successive CPETs, separated by 24 hours. EVs will be characterized in blood samples taken at four different time points, preDay1, postDay1, preDay2, and postDay2.

Extracellular vesicles (EVs), once ignored, are now receiving increasing attention as various roles in signaling in cancer, nervous system disorders, innate immunity, pregnancy, and stress responses have become evident [1,2]. Several types of extracellular vesicles have been described, as well as identifying markers [1]. Exosomes, a specific type of EV, are small membrane-bound vesicles that are 30-120 nm in diameter that are released into the extracellular environment by various cell types when internal bodies fuse with the plasma membrane. Exosomes contain cargo such as proteins, lipids, hormones, and RNAs (especially miRNAs) that can influence the function of the cells with which they fuse. One possibility is that exosomes and other types of EVs are involved in cell-to-cell signaling that results in abnormalities in ME/CFS patients' immune function and metabolism at baseline but particularly after any exertion (see Figure 1). In healthy individuals, exercise is known to result in the release of exosomes [3], but there are no published studies on the effect of exercise on EVs in ME/CFS. The size distribution and concentration of isolated exosomes/EVs will be performed using Nanoparticle Tracking Analysis on the Malvern NS300 Nanosight instrument.

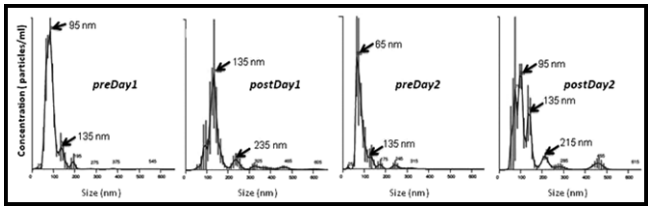

Figure 2: Changes in EV size distribution before and after two exercise challenges on consecutive days, as measured by Nanoparticle Tracking Analysis.

Summary of Research:

We examined EV size and concentration in plasma from 35 ME/CFS patients and 35 healthy controls. By performing NTA with the Malvern NS300 Nanosight, we found that the concentration of the exosome size class was increased in the patient plasma, though the concentration of the total EV population was not significantly different. The aforementioned plasma was collected the same day as the blood draw. We used a second population in which blood was shipped overnight before plasma was collected.

In this second population, we observed that the concentration of all size classes of EVs and the average size of the EVs were significantly increased in the patient plasma. A pilot experiment with blood taken at four time points in shown in Figure 2 and demonstrates the expected increase in size and concentration after exercise.

References:

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