A Case-Series Study of Autonomic Nervous System Functioning in a Long Covid patient, a ME-CFS, and a Healthy Control Subject (ID 2828).

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ABSTRACT

- There has been concern about possible long-term sequelae of COVID19 infection resembling Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) in COVID-19 patients. Post-infectious, myalgic encephalomyelitis/chronic fatigue syndrome (ME_CFS) symptoms have been widely observed in COVID-19. It is suggested that Long COVID, or post-COVID syndrome (PCS), like CFS, may be related to a virus-or immune-mediated disruption of the autonomic nervous system (ANS) (Dani et al., 2021). HRV measures assessing the capacity of healthy regulation of the ANS, muscle tonus measurements showing muscle tension status, and Diffusion Tensor Imaging of central brain pathways may show biomarker qualities for ME/CFS and LongCovid

BACKGROUND

- A recent review of lessons learned from past epidemics suggests that potential long-term health complications may be associated with COVID-19 (Islam et al., 2020). There has been concern about possible long-term sequelae resembling Myalgic Encephalomyelitis/Chronic Fatigue Syndrome in COVID-19 patients (Wostyn, 2021). Post-infectious, chronic fatigue syndrome (CFS) symptoms have been widely observed in COVID-19 and other viral and non-viral infections (Islam et al., 2020). It is suggested that COVID-19, like CFS, may be related to a virus-or immune-mediated autonomic nervous system disruption (Dani et al., 2021). Chronic fatigue syndrome (CFS) is a complicated disease characterized by extreme fatigue that rest cannot relieve. Amongst its significant symptoms are post-exertion malaise (PEM), sleep dysfunctions, pain, neurological/cognitive manifestations, and deficits found in autonomic-, neuroendocrine-, and immune system functioning (Holgate et al., 2011; Komaroff, 2017 2019).

- Long COVID, or post-COVID syndrome (PCS), is not a single condition and has been defined by the National Institute for Health and Care Excellence (NICE) as “signs and symptoms that develop during or following an infection consistent with COVID-19 which continue for more than 12 weeks and are not explained by an alternative diagnosis.”

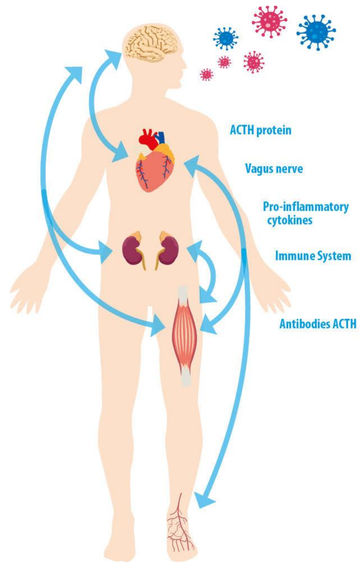
- Hypercortisolism is found in CFS populations and, more recently, also in COVID-19 populations (Heidarpour et al., 2020; Mongioì et al., 2020; Nijhof et al., 2014; Pal & Banerjee, 2020; Tak et al., 2011; Tanriverdi et al., 2007). As such, an urgent investigation of Long Covid is needed. Testable hypotheses derived from recent Long Covid literature (Dani et al., 2021; Goldstein, 2020). Those biomarkers of autonomic nervous system activation could correlate with clinical and pathophysiologic data and could act as prognostic markers in both CFS and Long Covid disease trajectory and recovery.

OBJECTIVES

- The functioning of, and flexibility (homeostasis) of, the cardiovascular and neuromuscular systems was examined using Heart Rate variability analysis, Micro-vibrational System (MVS) assessment (measured as skeletal muscle tone during rest), and oxygen saturation. The objective was to measure to what extent and how stress processes affect bodily systems. Heart Rate Variability (HRV) is a non-invasive procedure: It permits an objective/quantitative assessment of the capability of the cardiovascular system to regenerate itself. It also gives an empirical insight into the functioning of the autonomic nervous system. As a rule, less variability/ oscillation in heart rhythm indicates higher stress on the heart and the organism. The Micro-vibrational System (MVS), defined as skeletal muscle tone during rest, is a method developed by Prof. Peter Weinberg and Dr. Christof Ziaja at the Institute for the Science of Sport, University of Hamburg, in cooperation with the Olympic Centre in Hamburg. MVS analysis informs us about the energetic efficiency of muscular cooperation. An inefficient collaboration leads to permanent tension (a heightened muscular tone) and thus to overall exhaustion, permanent tension of muscular groups, and imbalances and blockages of muscles and joints.

METHODS

- This case study series examined cardiovascular and neuromuscular systems functioning using Heart Rate Variability (HRV) analysis (in the supine position) and Micro-vibrational System (MVS) analyses Hz of musculoskeletal silent tremor and the Nerve Express HRV System, Kubios HRV, and the Faros 180 Sensor and analyses software. Low Frequency (LF) (0.04 Hz - 0.15 Hz) and very/ultra-LF (VLF/ULF; 0.015 Hz - 0.04 Hz) correspond to a hypothalamic-pituitary axis stress response and sympathetic nervous system activation (Post/Pre Ganglion-Cells- and A/Delta C-Fiber). ME/CFS and PCS diagnoses were established using a combination of clinical diagnosis, self-report measures, and ICD-10 coding.

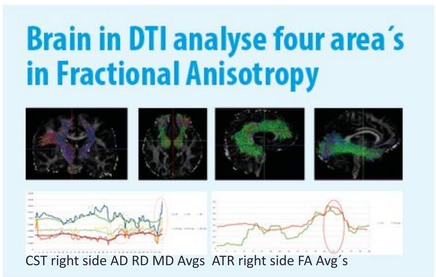


- Fig. 1 Shows the corresponding pathways of influence and interaction of EBV and SARS-Covid II from top to down.

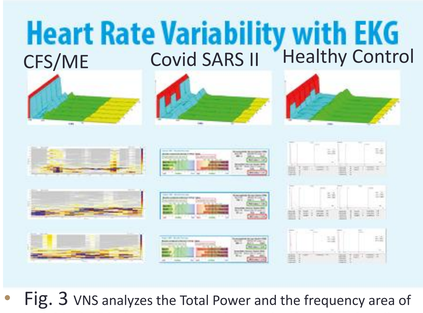
RESULTS

- The 3 participants were female (Age *M*= 50, *sd*= 5) and measured at rest for 30-45 minutes in the supine position. HRV measurements of both the PCS and ME/CFS patients showed high sympathetic nervous system activation (LF and VLF/ULF ranges), specifically, the LF bandwidths (Long Covid; 0.02 - 0.15 Hz; EDR <0.2, ME/CFS, LF= 0.02-0.23 Hz, EDR= 0.15-0.23). Additionally, the PCS patient showed a compression in the ULF range (ULF= 0.09-0.1 Hz, 71-85 resting heart rate), while the HC subject showed parasympathetic nervous system recruitment (0.25 Hz) after an 8-minute supine position. Low Total Power values PCS (Post Covid Syndromes) TP = 362 - 452 lying down with a pulse of 70-74 with a sympathetic graph represented by the red line with dots that remains at 1 / Parasympathetic green remains well below 0 line -2 to -1; the ME/CFS patient TP = 575 -280 lying down with a pulse of 79-89 (line red sympathetic >1 and parasympathetic <0 / -4) and the control person TP = 1679 -348 lying down with a pulse of 55-57 (line red sympathetic = 0 and parasympathetic = 0). A noticeable phase shift of the MV in both patients was noted compared to the HC. The cardiovascular and MV systems' interaction illustrates a burn-out-like state caused by high body tension. (High vibration = high entropy = low energy = chronic fatigue) Covid-19 patient MV = 14 Hz, ME/CFS MV = 13, control person MV = 6 Hz.

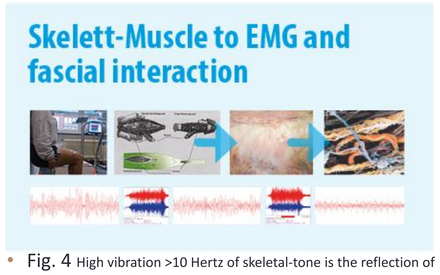
RESULTS



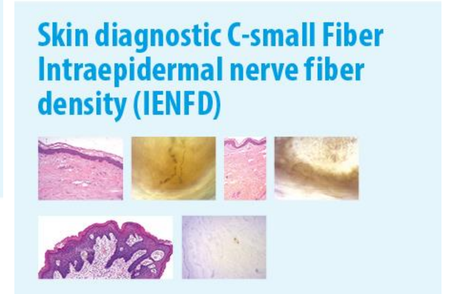
- Fig. 2 Shows from left to right ME/CFS Patients in CST (Corticolspinal tract) right Area **AD_Avg>0.01** the ATR (Thalamus) right **FA_Avg>0.7** AF (Arcuate Fasciculus) right **FA_Avg>0.4** and ILF (Inferior Longitudinal Fasciculus) right **FA_Avg>0.5.** Central Nerve System in DTI (Diffusion Tensor Imaging) analyzes four areas (AF=Acurate Fasciculus ATR=Anterior Thalamus Radiation CST=Corticol Spinal Tract ILF=Inferior Longitudinal Fasciculus) in fractional anisotropy (FA). FA is a quantitative value of diffusion anisotropy. It is used to set the threshold values for the termination of fiber tracking. Lower threshold values for FA show more details of fiber connections (see healthy control right side of the graphics). The income information of the thalamus to the motor cortex and sensory cortex, parts of the vagus nerve pathway, can´t handle the over stimulus of stress - influence of the virus in ACTH axe. With the help of functional imaging, a literalization concept of autonomous regulation could be proposed. Even the Thalamus plays a vital role in the interaction between micro-vibration (speed of contraction in Hertz) and muscle tone in Fig. 4; also in processing how the sympathicus workflow handle information from the right side of the Thalamus of the environment outside to inside in signal intensity process to the VNS.



- Fig. 3 VNS analyzes the Total Power and the frequency area of LF 0.04 - 0.15 in Sympathicotone interaction Post- Pre-Ganglion Cells. They are overheating because they try to find a way back into balance after high contraction following relaxation (long loop reflex). The cardiovascular interaction with the mechanoreceptors and Golgi-tendon-apparatus influences the pulse (BPM) and the intensity of the micro-vibration skeletal muscle. Ground Section of the micro-vibration signal in hertz (wave per second) measures the silent tremor from the musculus quadriceps and the EMG signal; it shows high vibration, high entropy, and low energy as a result of chronic fatigue because of a mechanism that disregulates the collagen in the fascial exchange of the interment of the fascial. This mechanism leads to pain in the muscle. The skeletal muscle encases the Golgi and muscle – spindles of the different interactions of the fascia, connective tissues, and the venous system to regulate blood pressure and the lymph system.



- Fig. 4 High vibration >10 Hertz of skeletal-tone is the reflection of cerebral cortex (Thalamus to motor cortex) excitement (Annochin et al.) to anticipating peripheral local micro-vibration (Rohracher et al.). These pathway areas are in a kind of overheating. They need more intensity to get through the brain’s pathways because of the damage to the axon or the reduced myelin sheath. This disturbance of fiber connectivity influences the intensity of contraction waves of the skeletal muscle's silent tremor (micro vibration Rohracher) as the ground state. These overstrain of high results of FA are compensation for body-mind interaction. The tremor is accelerated by stimulating the tegmentum of the caudal hypothalamus of the lateral core, the tractus mamillothalamicus. The micro vibration also behaves in the same way. The tremor disappears after the caudal hypothalamus's destruction and after the spinal cord's removal; in this case, the micro-vibration also stops. The right hemisphere's insular cortex appears to strongly influence sympathetic cardiovascular function, while the left hemisphere acts more on parasympathetic function. The hypothalamus is the most crucial control center for both parts of the autonomic nervous system (Cechetto et al., 2009).



- Fig. 5 Shows a reduction of C-Fiber and A delta fiber neuropathy. It leads to autonomic dysfunction POTS (postural tachycardia syndrome). High skeletal muscle Hertz results from no communication pathway of fascial disorder. On the left side, the CFS/ME patient with reduced nerve fibers by number **12 PgP9.5**; in the middle section, the Long Covid patients with **19 PgP9.5** nerve fibers and on the right the healthy control with **177 PgP9.5** nerve fibers. Intraepidermal nerve fiber density (IENFD) normative values for clinical use at age 40-49 should be **70 PgP9.5.**

CONCLUSIONS

- In line with an emerging body of research, our comparisons of cardiovascular and musculoskeletal outcomes of the two patient subjects show comparable rates of autonomic nervous system dysregulation, increased skeletal muscle tone, and decreased oxygen saturation compared to the healthy control subject. Further research about autonomic dysregulation in PCS and ME/CFS is thus warranted.