Advancing Therapeutics for Post-Viral ME/CFS and SFN in Long COVID: **A 20-Week Sensomotoric Training Intervention**

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ABSTRACT

- **Introduction:** Long COVID's (LC) emergence drives research and novel treatments for myalgic encefalitis ME/CFS. Sensomotoric-training's potential to regenerate ectodermal fibers offers hope for SFN patients.
- **Research Focus:** Long COVID's surge prompts innovative ME/CFS treatments targeting underlying causes. Sensomotoric-training's fiber regrowth potential could transform SFN management.
- **Conclusion:** Rising ME/CFS cases from Long COVID fuel research and therapeutic progress. Sensomotoric-training holds promise for SFN treatment. Exciting developments shape patient care.

METHODS

- This study involved **10 female patients with Small Fiber Neuropathy (SFN),** with an average age of 38 years (SD = 5 years). The study focused on demographic and clinical data, disability levels, and skin biopsy results displaying reduced C-Fibers. The intervention comprised 10 exercises per session, three times weekly, over 20 weeks. A second skin biopsy occurred after this period, with each exercise involving 3 repetitions lasting 20 seconds.
- **Skin biopsies were taken 7 to 10 centimeters** above the left ankle (lateral Malleolus) using methodologies from Lauria et al. (2005). Post 20 weeks, another skin biopsy was performed at the same location. Two labs were utilized: UKGM Giessen and Marburg, and UKE Neuropathology Lab of Hamburg.
- **Participants completed 10 sensorimotor balance exercises**, each lasting 20 seconds with a 1-minute break, both on solid ground and a soft mat. Exercise details, such as pace and intensity, were personalized. A soft floor mat was provided for exercise execution.

RESULTS

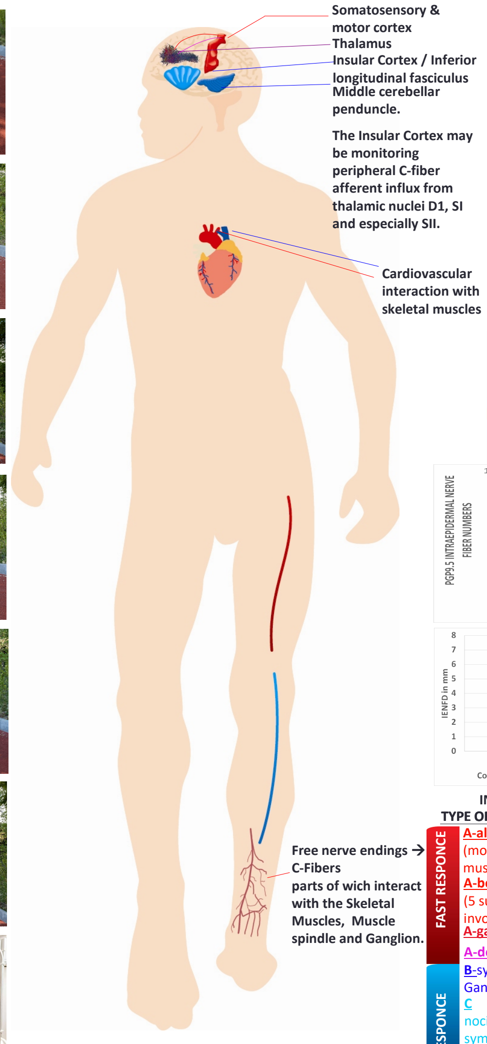
- **Between biopsies**, a notable increase of 5 to 56 percent in the count of C-Fibres was observed. Participants reported reduced balance challenges, heightened dexterity, and improved reaction times. A comparison group undergoing no exercises displayed a decrease in C-Fibre numbers after 20 weeks. Females aged 30-39 typically exhibit intraepidermal nerve fibre density values of 7.1-12.4. While nerve fibre density (IENFD) did not significantly improve and remained partly unchanged, a positive development manifested in increased C-fibre density and number (e.g., 1.8mm nerve fibre density and 12 PgP9.5 positive intraepidermal nerve fibres before intervention → after 20 weeks of exercise = 3.2mm / a 56.25% increase in nerve fibre density and 54 PgP9.5 / a 22.22% increase in positive intraepidermal nerve fibres), yet still slightly below the normal range for age.
- Certain **participants encountered** enhanced balance, reduced perspiration, increased strength, and diminished hand and foot pain. Some patients experienced severe nausea during exercises, leading to their exclusion from the study. Even on challenging days, they persisted with brief exercises lasting 5-10 seconds. Subjectively, dexterity and coordination improved over time. Influences from the Insular cortex, Inferior longitudinal fasciculus, cerebellum, and caudal thalamus were found to be significant. The tractus mamillothalamic core governed the modulation of microvibration tremor speed of skeletal muscles (refer to Fig. 1, assessed through Jump tests pre and post-exercise, with varied delay timings).

CONCLUSIONS

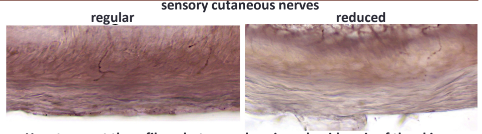
- **This Exercise based intervention offers significant therapeutic potential for ME/CFS and LC patients.** Future research should explore broader aspects, investigating the impact of balance and sensory exercises on other affected biological systems in CFS/ME. Despite promise, the potential remains underestimated and requires deeper comprehension. More patient data is essential for result validation.

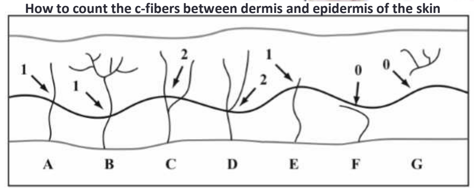
RESULTS

Fig. 1 Top down shows 10 different Exercise forms of sensomotoric training. A jump test has to be performed before and after 20 weeks of intervention to measure the balance quality of supraspinal control and its coupling properties.



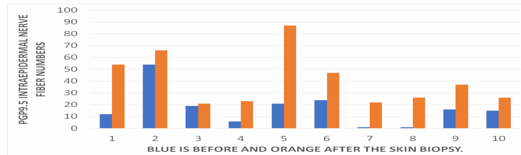
- Fig. 2 Shows the connections between the central, vegetative and neuromuscular systems.





Intraepidermal nerve fiber density (IENFD) normative values for clinical use

Age (years)	Females (n = 285) Number of subjects	Females 0.05 Quantile IENFD values per age span	Females Median IENFD values per age span	Males (n = 265) Number of subjects	Males 0.05 Quantile IENFD values per age span	Males Median IENFD values per age span
20–29	57	8.4	13.5	36	6.1	10.9
30–39	47	7.1	12.4	40	5.2	10.3
40–49	70	5.7	11.2	62	4.4	9.6
50–59	59	4.3	9.8	53	3.5	8.9
60–69	32	3.2	8.7	43	2.8	8.3
70–79	16	2.2	7.6	22	2.1	7.7
≥80	4	1.6	6.7	9	1.7	7.2



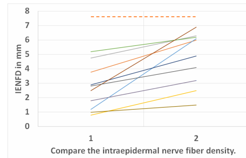


Fig. 4 From top to bottom shows the procedure of laboratory diagnostics and counts the stained nerve fibers PgP9.5. The neuropeptide protein product visualizes the thin nerve fiber and shows the age-related classification of nerve density in the table below.

INFORMATION CARRIED BY FIBER

	TYPE OF FIBER	FIBER IN ACTION
FAST RESPONCE	A-alpha 10-20µm (motor to skeletal muscles* silent tremor)	Vibration
		Movement
	A-beta 7-15µm (5 subtypes involved in touch)	Indentation
		Stretch
	A-gamma* 4-8µm	Movement of longer hairs
	A-delta 2-5µm	
SLOW RESPONCE	B-sympath. pre-Ganglionic 1-3µm	Movement of shorter hairs (unpleasant)
	C 0,1-1,5µm nociception sympath. post-ganglionic (1 subtype involved in touch)	Movement of shorter hairs (pleasant)
		Temperature

- Fig. 3 Classification of nerve fibers.

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