Case Report

Whole-Body Cryostimulation in Functional Neurological Disorders: A Case-Report

Federica Verme * , Jacopo Maria Fontana , Paolo Piterà , Angelo Alito , Silvia Saffioti , Gabriele Baccalaro , Giuliano Zebellin , Paolo Capodaglio

Posted Date: 16 October 2023

doi: 10.20944/preprints202310.0937.v1

Keywords: chronic pain; conversion disorder; functional neurological disorders; rehabilitation; whole-body cryostimulation

Case Report

Whole-Body Cryostimulation in Functional Neurological Disorders: A Case-Report

Federica Verme [1]*, Jacopo Maria Fontana [1], Paolo Piterà [1], Angelo Alito [2], Silvia Saffioti [1], Gabriele Baccalaro [1], Giuliano Zebellin [1] and Paolo Capodaglio [1,3]

[1] Research Laboratory in Biomechanics, Rehabilitation and Ergonomics, Istituto Auxologico Italiano, IRCCS, San Giuseppe Hospital, 28824 Piancavallo (VB), Italy; f.verme@auxologico.it; j.fontana@auxologico.it; p.pitera@auxologico.it; silviasaffioti7@gmail.com; g.baccalaro@auxologico.it; ; g.zebellin@auxologico.it; p.capodaglio@auxologico.it

[2] Department of Biomedical, Dental Sciences and Morphological and Functional Images, University of Messina, 98125 Messina, Italy; alitoa@unime.it

[3] Department of Surgical Sciences, Physical Medicine and Rehabilitation, University of Torino, 10126 Torino, Italy; p.capodaglio@auxologico.it

* Correspondence: f.verme@auxologico.it

Abstract: Functional neurological disorders (FND) are relatively frequent disabling conditions. Given their complexity, multidisciplinary rehabilitation is envisaged. Whole-body cryostimulation (WBC) represents a promising adjuvant treatment, mainly because of its anti-inflammatory and exercise-mimicking effects. Here, we propose a novel use of WBC in a wheelchair-ridden 61-year-old woman diagnosed with FND and other comorbidities, who, after several therapeutic and rehabilitation failures, underwent a multidisciplinary rehabilitation program including WBC. The 4-week program included physiotherapy, nutritional intervention, psychological support, and WBC. Questionnaires to assess disease impact, pain level, perceived fatigue and sleep quality were administered. At discharge, improvements in body composition, haematological biomarkers, physical performance, and questionnaire scores were observed. The patient was able to walk with a walker for medium distances, even outdoors. We observed unprecedented improvements, particularly in functional parameters and questionnaire scores. Although we cannot ascertain to which extent WBC *per se* contributed to the improvements measured, subjective reporting and our clinical observation were that WBC, the only intervention not previously experienced by the patient, acted as a booster for the rehabilitation interventions. Further research will be necessary to rule out any possible placebo effect and to assess the effects of WBC on FND.

Keywords: chronic pain, conversion disorder, functional neurological disorders, rehabilitation, whole-body cryostimulation.

1. Introduction

Functional neurological disorders (FND) (also called conversion disorder or functional neurological symptom disorder) are relatively common problems in neurologic practice. The diagnosis is based on findings in the neurological examination demonstrating that the symptom lasting for at least 6 months is incompatible with a structural neurological illness [1]. In FND, the cardinal symptom is limited solely to neurological symptoms: alterations in voluntary motor, cognitive, or sensory function that are not compatible with any recognized neurological condition. The clinician must establish evidence of preserved physiological function despite the presence of a neurological symptom. Disability in FND is similar as in structural disease, and neurological outcome at 8 months is poor, with over 50% of patients showing no improvement [1]. Among therapeutic options, multidisciplinary rehabilitation is an important component of symptomatic and supportive treatment for FND [2]. Participation in a treatment process that changes "the way the brain processes information" is essential to minimise the tendency to express distress through physical symptoms. Physiotherapy and physical therapies are a first line treatment for patients with motor FND and have the goal to change the processing of complex motor programs and to facilitate engagement in more

 doi:10.20944/preprints202310.0937.v1

adaptive patterns of movement. There is evidence that they are helpful in treating the motor and gait manifestations of FND [3,4]. Clinical judgement should be used as to when it is appropriate to initiate medications to treat comorbid psychiatric conditions and psychotherapy. Cognitive-behavioural therapy has been shown to be beneficial in treating FND, and a variety of other psychotherapies have been proposed [2,5]. Patients with FND require an integrated multidisciplinary approach and the intensity and the educational component of the program appear to be an important factor for success.

Whole-body cryostimulation (WBC) is a physical treatment where the entire body is exposed to cryogenic temperatures (−110 ◦C to −140 ◦C) for 2–3 minutes. Exposure to these temperatures are able to reduce pain and inflammation improving several metabolic parameters (thermogenesis, lipid profile, insulin sensitivity, and glucose utilisation), as well as depression, anxiety, and sleep quality [6–10]. Furthermore, cycles of WBC can reduce fatigue and disease activity in patients with several conditions, such as multiple sclerosis [11], post-COVID-19 condition [12], rheumatoid arthritis [13], polymyalgia rheumatica [14], and fibromyalgia [15,16]. To the best of our knowledge, no studies have so far investigated the effects of WBC on FND.

2. Detailed Case Description

T.C., 61year-old woman, wheelchair-ridden for the last year, was admitted to our Unit for a multidisciplinary rehabilitation (MR) program with the following diagnoses: FND, polyarthralgia (particularly lumbar spine with disc protrusions and knee arthritis), widespread myalgia, sleep disorder, morbid obesity, arterial hypertension, urinary incontinence, gastroesophageal reflux.

Medical history. After the age of 18, the patient progressively gained weight. In 2013, she experienced distress due to an abrupt dismissal from work: physical activity levels dropped dramatically and eating behaviour became dysfunctional. She was diagnosed with dysthymia and reactive anxiety for which psychological support, benzodiazepines and selective serotonin reuptake inhibitors were prescribed, with no subjective benefit.

In 2017, her very dear brother passed away because of Amyotrophic Lateral Sclerosis. Later, she showed up at the Emergency Department for atypical chest pain, diagnosed as an anxiety disorder. The following year she was complaining of distal motor deficit in her upper arms and sleep disturbances. EMG and EEG evaluations excluded polyneuropathy, and antidepressants and pregabalin were prescribed with psychological support. Because of persisting pain in her hands, wrists, and spine, she underwent rheumatological/immunological examinations, spinal MRI, bone scintigraphy, DEXA and human leukocyte antigen B27 (HLAB27) testing. No signs of autoimmune or systemic inflammatory conditions were present. MRI of the lumbar spine documented diffuse discopathies with left L2L3 intraforaminal protrusions, narrowing of the spinal canal at L3L4 and L4L5, and thickening of the yellow ligaments. Bone scintigraphy revealed polyarticular bone edema, juxta-articular osteoporosis, and enthesopathy of the achilles and plantar fascia. DEXA and immunological tests were normal. A diagnosis of fibromyalgia was formulated, and anti-inflammatory medications prescribed.

In April 2021, she underwent a neurological examination due to difficulty walking with weakness, “freezing” and “rigidity” of the lower limbs and widespread pain. The EMG results were normal. MRI of the brain revealed a Dandy-Walker malformation. Neuropsychological tests revealed mild memory and praxic impairments in both the visual-spatial and episodic anterograde components, with a normal Mini-Mental State Examination (MMSE) score. The diagnosis of fibromyalgia was confirmed.

In May 2021, she presented to the emergency room for motor deficit in the left side of the body, clonus in the left part of the face, dysarthria, and oral rhyme deviation. CT scan and neurological examination were negative. She was diagnosed with possible conversion disorder. In August 2021, a neurological examination confirmed the diagnosis of FND. Since then, she has been followed by the Psychiatric Unit of the Milan Polyclinic. Pharmacological therapy with duloxetine was prescribed, combined with a rotation of other medications (topiramate, benzodiazepines). Since January 2022, stress urinary incontinence with detrusor hyperactivity and low compliance bladder with interrupted flow were established, for which sanitary pads were prescribed. In June 2022, EEG showed global

 doi:10.20944/preprints202310.0937.v1

minimal slowing of the electric cerebral activity with an excess of slow intermittent activity in the frontal-temporal site. For knee pain, she underwent MRI, which documented presence of intra- and extra-articular swelling in reactive arthrosynovitis, complete lateral and medial meniscus lesion, Baker's cyst, for which physiotherapy was performed with no significant gain. Walking was only possible for a few steps with double support and bilateral steppage and she reported to have been confined to a wheelchair since then.

In January 2023, difficulty in sit-to-stand was evident. Obesity was also present. She unsuccessfully underwent outpatient physical therapy and weight management interventions. In July 2023, the presence of signs of cortical release (palmar-mental and muzzle-glabellar reflexes) and EEG findings required further investigations to rule out possible frontal-temporal dementia, but a PET/CT scan revealed no significant abnormalities. Neuropsychological assessment revealed a normal MMSE score (24/30) but working and short-term memory (verbal and visual-spatial) appeared slightly reduced. She was needing assistance with dressing/undressing and personal hygiene. The family doctor recommended to undergo an inpatient multidisciplinary rehabilitation program with the aim of reducing body weight and improving independence in daily activities, which she willingly accepted.

Clinical Examination. At admission in our Rehabilitation Unit, she presented with morbid obesity (body weight 113.2 kg, height 167 cm, BMI: 40.5) and lipo-lymphedema in her lower limbs. She complained of diffuse pain and weakness, fibromyalgia trigger points were positive, sit-to-stand was performed slowly only with direct assistance, she was able to move a few steps with assistance and double support and bilateral steppage and dyspnoea was evident after light effort. Muscular strength in the upper limbs (Mingazzini I manoeuvre) was bilaterally reduced, but when verbally encouraged she was able to hold the position for 15 seconds. Muscular strength in the lower limbs (Mingazzini II manoeuvre) was frankly reduced, but, again, if verbally encouraged, was able to hold the position for 10 seconds. Other central or peripheral neurological signs were absent. Spinal digital compression was painful and the articular range of motion in the lower limbs was limited mostly because of excessive adiposity. Segmentary strength was difficult to assess because of the lack of voluntary recruitment of muscles on demand, whereas, in the functional context, specific muscles were activated. Overall, the clinical picture showed functional limitation secondary to multifactorial aetiology in chronic-degenerative pain, psychiatric component, fibromyalgia syndrome and morbid obesity.

Rehabilitation interventions. The following interventions were planned progressively during a 4-week hospital stay: mobilisation of the 4 limbs and girdles, low-intensity arm ergometer exercises to increase aerobic capacity and exercise tolerance, gradual isometric and isotonic muscle strengthening aimed at functioning in daily life , drainage techniques and pressure therapy for lower limbs lymphedema, proprioceptive exercises, training of postural transfers, trunk balance, sit-to-stand, aids-assisted standing, and walking. Physical therapies (TENS at spinal level, TECAR at knee level) were also provided. Psychiatric/psychological support was provided for education and awareness of possible correlations among depressive symptoms, chronic pain, obesity and functional syndromes along with behavioural therapy for pain management, monitoring of mood, sleep, pain and eating behaviour with caregivers' involvement.

Nutritional intervention. A 1300 kcal diet, divided into three meals and composed as follows: 70 g protein (21%), 42 g lipids (29%) and 162 g carbohydrates (50%).

WBC. The patient underwent a total of 9 daily WBC sessions in a cryo-chamber (Artic, CryoScience, Rome) where she was exposed at −110 ◦C for two minutes. Before starting the treatment, the patient underwent a medical examination to rule out any contraindications according to Bad Voslau's guidelines [17].

Outcome measures. Anthropometrics and body composition (body weight, body mass index (BMI), fat mass (FM) and fat-free mass (FFM)), haematological biomarkers, and physical performance tests were measured before and after the completion of the rehabilitation program. We performed the Functional Independence Measure (FIM) [18], the Timed Up and Go test (TUG) and the Visual Analogue Scale (VAS) for pain and disability. The patient was also asked to fill in several validated

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 16 October 2023 doi:10.20944/preprints202310.0937.v1

questionnaires. The Revised Fibromyalgia Impact Questionnaire (FIQR) [19], the Fatigue Severity Scale (FSS) [20], a numeric rating scale for pain (NPRS) [21], the Central Sensitization Inventory (CSI) [22], the Brief Pain Inventory (BPI) [23], the Depression Anxiety Stress Scales-21 (DASS-21) [24], the World Health Organisation - Five Well-Being Index (WHO-5) [25], the Pittsburgh Sleep Quality Index (PSQI) [26].

Results. After the comprehensive rehabilitation program, the patient achieved adequate weight loss, improved trunk mobility, and was able to walk medium distances with a 4-wheel walker, even outdoors. All indicators considered improved (see Table 1), and the questionnaire scores showed a clear improvement in the patient's disease impact, fatigue, pain, general state of well-being, and sleep quality (see Table 2).

Table 1. Pre-post total scores and percentage change of anthropometric measurements (body weight, BMI, FM and FFM) and functional indicators (FIM, TUG, VAS pain lower limbs and lumbar spine, VAS disability, trunk mobility). The percentage change (Δ%) was calculated using the formula: Δ% = (POST−PRE)/PRE × 100.

Anthropometric measurements				
		PRE	**POST**	**Δ%**
Body weight (kg)		113.2	107	-5.48
BMI (kg/m2)		40.5	38.3	-5.43
FM (%)		56	54.1	-3.39
FFM (%)		43.7	45.9	5.03
Functional indicators				
		PRE	**POST**	**Δ%**
FIM		96	109	13.54
TUG		38.05	20.22	-46.86
VAS	**Pain (Lower limbs)**	80	40	-50.00
	Pain (Lumbar spine)	90	50	-44.44
	Disability	100	70	-30.00
Trunk	**Bending (°)**	40	70	75.00
	Extension (°)	5	10	100.00
	Left Inclination (°)	10	15	50
	Right Inclination (°)	10	15	50

Table 2. Pre-post total scores and percentage change of Questionnaire (FIQ, FSS, NPRS, CSI, BPI, DASS-21, WHO-5 and PSQI) scores. The percentage change (Δ%) was calculated using the formula: Δ% = (POST−PRE)/PRE × 100. .

Questionnaires (Total Scores)				
		PRE	**POST**	**Δ%**
FIQR		71.83	26.33	-63,34
FSS		33	15	-54,54
NPRS		9	1	-88,89
CSI		42	23	-45,24
BPI	**Pain Severity**	5.75	1.75	-69,56
	Pain Interference	5.43	2.29	-57,83
DASS-21	**Depression**	10	6	-40
	Anxiety	10	4	-60
	Stress	12	6	-50
WHO-5		72	88	22,22

 doi:10.20944/preprints202310.0937.v1

PSQI	12	8	-33,33

3. Discussion

This is the first case-report using WBC in a patient with FND. Previous "off label" prescriptions of WBC (i.e., post-COVID-19 condition, polymyalgia rheumatica), have shown positive effects, likely due to the wide range of effects elicited by WBC on pain, fatigue, mood [12,14,27]. WBC is a powerful physical modality that represents an intense physical experience for the patient. The patient's positive emotional involvement in the treatment and a highly rated satisfaction may have played a role in the global functional improvement observed and a placebo effect cannot be ruled out. More importantly, we cannot ascertain to what extent WBC *per se* may have contributed to the outcomes, since the patient underwent a comprehensive rehabilitation program including nutrition, physiotherapy, psychological support on top of WBC. However, the patient's subjective perception was that, from the very early sessions, WBC provided rapid sensation of well-being and reduced perception of fatigue and pain. The tests carried out showed unprecedented improvements, particularly in physical performance, to the point where she no longer needed a wheelchair for mobility, as well as in symptoms related to pain, fatigue, sleep quality and well-being. Our clinical speculation is that WBC, a treatment never experienced by the patient before, may have acted as a booster for rehabilitation interventions. Controlled studies will have to confirm this report.

Author Contributions: Conceptualization, F.V., P.C., and J.M.F.; methodology, G.Z., G.B., P.C.; validation, F.V. and J.M.F.; formal analysis, F.V.; investigation, F.V., P.C., P.P., A.A and S.S.; resources, F.V., P.P., G.Z. and G.B.; data curation, F.V., P.P., S.S. and P.C.; writing—original draft preparation, F.V. and P.C.; writing—review and editing, F.V., P.C., J.M.F., A.A.; visualization, F.V.; supervision, P.C. and J.M.F.; funding acquisition, P.C. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by Italian Ministry of Health - Ricerca Corrente.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of Istituto Auxologico Italiano (protocol code 2021_05_18_14, approved 18 May 2021).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available within the article.

Acknowledgments: In this section, you can acknowledge any support given which is not covered by the author contribution or funding sections. This may include administrative and technical support, or donations in kind (e.g., materials used for experiments).

Conflicts of Interest: The authors report no conflict of interest. The authors alone are responsible for the content and writing of the article.

References

1. Stone, J.; Carson, A.; Sharpe, M. Functional Symptoms and Signs in Neurology: Assessment and Diagnosis. *J Neurol Neurosurg Psychiatry* **2005**, *76 Suppl 1*, i2-12, doi:10.1136/jnnp.2004.061655.
2. Aybek, S.; Perez, D.L. Diagnosis and Management of Functional Neurological Disorder. *BMJ* **2022**, *376*, o64, doi:10.1136/bmj.o64.
3. Kaur, J.; Garnawat, D.; Ghimiray, D.; Sachdev, M. Conversion Disorder and Physical Therapy.; October 1 2012.
4. Ness, D. Physical Therapy Management for Conversion Disorder: Case Series. *J Neurol Phys Ther* **2007**, *31*, 30–39, doi:10.1097/01.npt.0000260571.77487.14.
5. Sharpe, M.; Walker, J.; Williams, C.; Stone, J.; Cavanagh, J.; Murray, G.; Butcher, I.; Duncan, R.; Smith, S.; Carson, A. Guided Self-Help for Functional (Psychogenic) Symptoms: A Randomized Controlled Efficacy Trial. *Neurology* **2011**, *77*, 564–572, doi:10.1212/WNL.0b013e318228c0c7.
6. Fontana, J.M.; Gobbi, M.; Piterà, P.; Giusti, E.M.; Capodaglio, P. Whole-Body Cryostimulation in Fibromyalgia: A Scoping Review. *Applied Sciences* **2022**, *12*, 4794, doi:10.3390/app12094794.
7. Alito, A.; Quartarone, A.; Leonardi, G.; Tisano, A.; Bruschetta, A.; Cucinotta, F.; Milardi, D.; Portaro, S. Brown Adipose Tissue Human Biomarkers: Which One Fits Best? A Narrative Review. *Medicine (Baltimore)* **2022**, *101*, e32181, doi:10.1097/MD.0000000000032181.

8. Fontana, J.M.; Bozgeyik, S.; Gobbi, M.; Piterà, P.; Giusti, E.M.; Dugué, B.; Lombardi, G.; Capodaglio, P. Whole-Body Cryostimulation in Obesity. A Scoping Review. *J Therm Biol* **2022**, *106*, 103250, doi:10.1016/j.jtherbio.2022.103250.
9. Rymaszewska, J.; Ramsey, D.; Chładzińska-Kiejna, S. Whole-Body Cryotherapy as Adjunct Treatment of Depressive and Anxiety Disorders. *Arch Immunol Ther Exp (Warsz)* **2008**, *56*, 63–68, doi:10.1007/s00005-008-0006-5.
10. Bouzigon, R.; Ravier, G.; Dugue, B.; Grappe, F. THE USE OF WHOLE-BODY CRYOSTIMULATION TO IMPROVE THE QUALITY OF SLEEP IN ATHLETES DURING HIGH LEVEL STANDARD COMPETITIONS. *Br J Sports Med* **2014**, *48*, 572.1-572, doi:10.1136/bjsports-2014-093494.33.
11. Miller, E.; Kostka, J.; Włodarczyk, T.; Dugué, B. Whole-Body Cryostimulation (Cryotherapy) Provides Benefits for Fatigue and Functional Status in Multiple Sclerosis Patients. A Case-Control Study. *Acta Neurol Scand* **2016**, *134*, 420–426, doi:10.1111/ane.12557.
12. Piterà, P.; Gobbi, M.; Fontana, J.M.; Cattaldo, S.; Massucci, M.; Capodaglio, P. Whole-Body Cryostimulation: A Rehabilitation Booster in Post-COVID Patients? A Case Series. *Applied Sciences* **2022**, *12*, 4830, doi:10.3390/app12104830.
13. Hirvonen, H.E.; Mikkelsson, M.K.; Kautiainen, H.; Pohjolainen, T.H.; Leirisalo-Repo, M. Effectiveness of Different Cryotherapies on Pain and Disease Activity in Active Rheumatoid Arthritis. A Randomised Single Blinded Controlled Trial. *Clin Exp Rheumatol* **2006**, *24*, 295–301.
14. Verme, F.; Scarpa, A.; Varallo, G.; Piterà, P.; Capodaglio, P.; Fontana, J.M. Effects of Whole-Body Cryostimulation on Pain Management and Disease Activity in Active Rheumatic Polymyalgia: A Case-Report. *Biomedicines* **2023**, *11*, 1594, doi:10.3390/biomedicines11061594.
15. Varallo, G.; Piterà, P.; Fontana, J.M.; Gobbi, M.; Arreghini, M.; Giusti, E.M.; Franceschini, C.; Plazzi, G.; Castelnuovo, G.; Capodaglio, P. Is Whole-Body Cryostimulation an Effective Add-On Treatment in Individuals with Fibromyalgia and Obesity? A Randomized Controlled Clinical Trial. *J Clin Med* **2022**, *11*, 4324, doi:10.3390/jcm11154324.
16. Vitenet, M.; Tubez, F.; Marreiro, A.; Polidori, G.; Taiar, R.; Legrand, F.; Boyer, F.C. Effect of Whole Body Cryotherapy Interventions on Health-Related Quality of Life in Fibromyalgia Patients: A Randomized Controlled Trial. *Complement Ther Med* **2018**, *36*, 6–8, doi:10.1016/j.ctim.2017.10.011.
17. Zimmer Medizin System. Consensus Declaration on Whole-Body Cryotherapy (WBCT). 2006.
18. Dodds, T.A.; Martin, D.P.; Stolov, W.C.; Deyo, R.A. A Validation of the Functional Independence Measurement and Its Performance among Rehabilitation Inpatients. *Arch Phys Med Rehabil* **1993**, *74*, 531–536, doi:10.1016/0003-9993(93)90119-u.
19. Sarzi-Puttini, P.; Atzeni, F.; Fiorini, T.; Panni, B.; Randisi, G.; Turiel, M.; Carrabba, M. Validation of an Italian Version of the Fibromyalgia Impact Questionnaire (FIQ-I). *Clin Exp Rheumatol* **2003**, *21*, 459–464.
20. Valko, P.O.; Bassetti, C.L.; Bloch, K.E.; Held, U.; Baumann, C.R. Validation of the Fatigue Severity Scale in a Swiss Cohort. *Sleep* **2008**, *31*, 1601–1607.
21. Alghadir, A.H.; Anwer, S.; Iqbal, A.; Iqbal, Z.A. Test–Retest Reliability, Validity, and Minimum Detectable Change of Visual Analog, Numerical Rating, and Verbal Rating Scales for Measurement of Osteoarthritic Knee Pain. *J Pain Res* **2018**, *11*, 851–856, doi:10.2147/JPR.S158847.
22. Chiarotto, A.; Viti, C.; Sulli, A.; Cutolo, M.; Testa, M.; Piscitelli, D. Cross-Cultural Adaptation and Validity of the Italian Version of the Central Sensitization Inventory. *Musculoskelet Sci Pract* **2018**, *37*, 20–28, doi:10.1016/j.msksp.2018.06.005.
23. Caraceni, A.; Mendoza, T.R.; Mencaglia, E.; Baratella, C.; Edwards, K.; Forjaz, M.J.; Martini, C.; Serlin, R.C.; de Conno, F.; Cleeland, C.S. A Validation Study of an Italian Version of the Brief Pain Inventory (Breve Questionario per La Valutazione Del Dolore). *Pain* **1996**, *65*, 87–92, doi:10.1016/0304-3959(95)00156-5.
24. Bottesi, G.; Ghisi, M.; Altoè, G.; Conforti, E.; Melli, G.; Sica, C. The Italian Version of the Depression Anxiety Stress Scales-21: Factor Structure and Psychometric Properties on Community and Clinical Samples. *Compr Psychiatry* **2015**, *60*, 170–181, doi:10.1016/j.comppsych.2015.04.005.
25. Topp, C.W.; Østergaard, S.D.; Søndergaard, S.; Bech, P. The WHO-5 Well-Being Index: A Systematic Review of the Literature. *Psychother Psychosom* **2015**, *84*, 167–176, doi:10.1159/000376585.
26. Buysse, D.J.; Reynolds, C.F.; Monk, T.H.; Berman, S.R.; Kupfer, D.J. The Pittsburgh Sleep Quality Index: A New Instrument for Psychiatric Practice and Research. *Psychiatry Res* **1989**, *28*, 193–213, doi:10.1016/0165-1781(89)90047-4.
27. Capodaglio, P.; Cremascoli, R.; Piterà, P.; Fontana, J.M. WHOLE-BODY CRYOSTIMULATION: A REHABILITATION BOOSTER. *J Rehabil Med Clin Commun* **2022**, *5*, 2810, doi:10.2340/jrmcc.v5.2810.