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Whole- and partial-body cryostimulation/cryotherapy: Current technologies and practical applications

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ABSTRACT

Cold therapy is commonly used as a method to relieve pain and inflammation. This review focuses primarily on two methods of cold therapy that have received recent attention: whole-body cryotherapy and partial-body cryotherapy. These methods are used to induce physiological and psychological benefits in humans in the context of medicine, health and sports. The subjects experiencing cryotherapy are dressed in minimal clothing and are exposed to very cold air (at −110 °C or less) for 1–4 min. Despite the increasing scientific interest in these methods, there is a lack of information about the technologies used. Moreover, there is no existing reference concerning exposure protocols and the relationship between temperature, duration, number of repetitions and the treatments' desired effects. The aim of this review is to compare whole- and partial-body cryotherapy effects (especially on skin temperature) and to classify the protocols for exposure according to the desired effects. This review emphasises 1) the lack of information concerning the actual temperatures inside the cabin or chamber during exposure and 2) the heterogeneity among the exposure protocols that have been reported in the scientific literature.

This review will be valuable and relevant to health professionals endeavouring to optimize the cold treatments offered to patients and producers of cryotherapy apparatus striving to create more efficient devices that meet market requirements.

Contents

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1. Introduction

The use of cold in medicine has been known since antiquity. In various ancient cultures, it was one of several traditional methods for relieving physical suffering. In ancient Greece, Persia and the Roman Empire, cold remedies such as snow, ice-water mixtures and cold water were applied to treat a wide range of diseases. In contemporary times, winter swimming—regularly taking a bath in ice-cold water during the winter season for health reasons—has become a popular practice in Nordic countries (Dugue and Leppanen, 2000). Winter swimmers believe that they become sick less often and that cold stimulation improves their ability to address with daily stress (Huttunen et al., 2004; Lubkowska et al., 2013). Today, cold application remedies are being developed in the medicine, health and sport domains. This review primarily focuses on two recent methods of cold therapy: whole-body cryotherapy (WBC) and partial-body cryotherapy (PBC). WBC and PBC are two methods that expose a patient to extreme cold for a short time, and both require a specialised cold chamber (cryochamber) or cabin (cryo-cabin). These methods are used to induce physiological and psychological benefits.

Little known a few years ago, these therapies have recently been the subject of tremendous interest. According to PubMed, there were approximatively 30 scientific studies concerning this topic before 2010 and there have been over 100 since then. The two most investigated domains are improvements in mental and physical health and improvements in recovery after physical exercise (Bleakley et al., 2014; Guillot et al., 2014). The populations studied include patients suffering from traumatologic, inflammatory or mental diseases, healthy individuals (no sport and no disease), and athletes (all levels) as well as active participants (moderate level of sport activity). In addition to the term “cryotherapy”, the term “cryostimulation” has emerged. Although the cold stimulation is the same, cryostimulation is targeted to subjects with no pathologies (e.g., healthy athletes), whereas cryotherapy involves patients.

Since the invention of PBC and WBC, several technologies for each have emerged and, there are approximately fifteen producers worldwide (Table 1). The differences between the two methods involve the exclusion of the head in PBC treatment, different ways to create cold, and different device sizes and mobility possibilities, which can attract different populations of users (Hausswirth et al., 2013). PBC uses a moderate-sized mobile device, whereas WBC employs a larger fixed device. Thus, PBC is used more in the field with sport teams, and WBC is used more often in rehabilitation or athletic sport centres.

The differences in the temperature of exposure inside the two devices are not clear. Currently, there is no standardised method of assessing these temperatures. The temperatures reported are those provided by the device producers. With the exception of three cryo-cabin models (Criomed, Kherson, Ukraine; Juka, Niepolomice, Poland; and Cryo Manufacturing, Perigny, France), in which temperatures are measured at the outlet of the nitrogen nozzle (Bouzigon et al., 2014; Savic et al., 2013), the site of assessment of cabins and chambers remains unknown. This lack of data is a problem for the validity of assessments in scientific research. It is not possible to know precisely what exposure temperatures were used in different studies. Furthermore, several articles (Tables 2–4) do not disclose the brand, model, producer and origin of the devices used in their materials and methods sections.

An interesting way to measure the efficiency of the different cryotherapy/cryostimulation technologies is to assess the variations in the cutaneous temperature induced by exposure. The strong variations in skin temperature induced by exposure to extreme cold lead to the stimulation of cutaneous thermoreceptors and therefore to the stimulation of the thermoregulation centre in the hypothalamus. The sympathetic adrenergic fibres are excited, which causes local arterioles and venules to constrict and reduces nervous conduction velocity (Herrera et al., 2010). Core and muscular temperature could also be affected. However, short cold exposure does not induce a large decrease in these temperatures immediately after treatment (Costello et al., 2012b; Westerlund et al., 2003).

WBC and PBC were first used to relieve rheumatic and inflammatory diseases such as rheumatoid arthritis (Hirvonen et al., 2006), fibromyalgia (Bettoni et al., 2013) or ankylosing spondylitis (Stanek et al., 2015). Currently, these methods are also being used in psychiatry to improve mental well-being, but there are only few studies on this topic. WBC and PBC treatments are used to relieve depression and anxiety syndromes (Rymaszewska and Ramsey, 2008). Previously, investigations in winter swimmers were performed to assess the effect of cold on well-being (Huttunen et al., 2004, 2001). In these studies, the adaption to cold was associated with a decrease in tension and fatigue and with an improvement in mood and memory. Winter swimmers reported feeling more vigorous, energetic, and active after a winter swimming period of four months (Huttunen et al., 2004). WBC and PBC were later used in the sports domain because cold exposure studies demonstrated their potential to enhance physical exercise recovery.

Though not completely clear, the mechanism leading to pain release and inflammatory symptom alleviation as well as recovery improvement after physical exercise appears to be related to cold-induced analgesia and cold-induced lower levels of oxidative stress and inflammation (Hausswirth et al., 2011; Leppaluoto et al., 2008; Pournot et al., 2011; Lubkowska et al., 2010; Lubkowska et al., 2012; Lubkowska et al., 2011). Cold stimulus reduces nerve conduction and acetylcholine formation (Bugaj, 1975). However, the stimulation of the sympathetic system, the release of noradrenalin and the vasoconstriction during and after the cold exposure may also have a significant impact on pain and joint and/or muscle soreness (Leppaluoto et al., 2008). Noradrenalin is released both from peripheral nerve endings and brainstem nuclei (Pertovaara et al., 1991). Moreover, noradrenalin spinal administration in animals and epidural injections of an adrenoceptor agonist in humans have been reported to alleviate pain (Pertovaara and Kalmari, 2003; Gordh, 1988). Circulating noradrenalin reaches the

Table 1
WBC and PBC technologies.

Technology	Manufacturer Model	Origin (Town, Country)	Temperature of exposure announced	Possible number of individual	CE medical/Class
PBC	Criomed PBC space cabin	Kherson, Ukraine	−120 to −170 °C	1	Yes (Unknown class)
PBC	Krion KAET-01	Saint-Petersburg, Russia	−130 to −190 °C	1	?
PBC	Cryo Manufacturing Cryocab	Perigny, France	−120 to −150 °C	1	?
PBC	Majestic Cryo Inc M-Cryo	Richardson, Texas, United States	Unknown	1	?
PBC	Asperia Group Cryoness	Gliwice, Poland	−110 to −160 °C	1	?
PBC	Impact Cryotherapy Octagon	Atlanta, Georgia, United States	−110 to −170 °C	1	?
PBC	Juka	Niepolomice, Poland	−140 to −160 °C	1	Yes, for both chambers
WBC			2 chambers: −40 to −60 °C and −100 to −160 °C	2–3 or 4–5	(Unknown class)
WBC	Zimmer Icelab	Neu-Ulm, Germany	2 or 3 chambers: −10 °C, −60 °C and −110 °C	1–4	Yes (Unknown class)
WBC	Mecotec Cryoair	Bitterfeld-Wolfen and Pforzheim, Germany	1 to 3 chambers: 1 chamber: −85 °C 2 or 3 chambers: −10 °C, −60 °C and −110 °C	1 3–4	Yes IIb and III
WBC	Kriosystem KR-2010S	Wroclaw, Poland	2 chambers: −60 °C and −110 to −160 °C	2–4	Yes (Unknown class)
WBC	Seilufreezer SMC-10	Chungcheongnam-do, South-Korea	2 chambers: −60 °C and −110 °C	2	?
WBC	Metrum Cryoflex Arctica Arctic cooling retention	Warsaw, Poland	1 to 2 chambers: −60 to −70 °C and −120 to −150 °C Open room placed in basement to keep the cold. Unknown temperature	2 or 2–4 2–3 or 4–6	Yes (Unknown class)
WBC	Stan Mar	Poznan, Poland	2 chambers: −60 °C and −120 °C	Unknown	Yes IIa
WBC	Creator Kriokomora	Wroclaw, Poland	2 chambers: −60 °C and −80 to −160 °C	2–3, 3–4 or 5–6	?

(Abbreviations: WBC, whole-body cryotherapy; PBC, partial-body cryotherapy).

spinal cord via the posterior spinal arteries supplying, for example, the substantia gelatinosa where pain afferents from skin terminate. A cold-induced increase in noradrenalin may therefore be involved in the mechanisms that lower pain at the spinal level. Moreover, several studies have reported that cold exposure induced a decrease in oxidative stress and/or an increase in anti-oxidative buffering capacities (Dugué et al., 2005; Lubkowska et al., 2008, 2009, 2010, 2015) as well as a decrease in inflammatory processes due to a lower production and release of pro-inflammatory substances and/or a higher production and release of anti-inflammatory compounds (Miller et al., 2010; Lubkowska et al., 2011; Lubkowska et al., 2015). Again, the mechanisms behind these adaptations are not completely understood at the current time. However, recent studies have suggested that adhesion molecules, such as intracellular adhesion molecule-1, may play a role in the cold-induced reduction of inflammation (Dugué, 2015; Ferreira-Junior et al., 2014a).

In the context of physical exercise, the process of skin and muscle cooling during and after cold exposure may also lower enzyme activities and metabolism; induce a peripheral vasoconstriction that reduces peripheral blood flow, thereby attenuating inflammatory response and the possible formation of oedema; and limit protein degradation after exercise-induced ischaemia, which can be an important feature of recovery improvement (Paddon-Jones and Quigley, 1997; Banfi et al., 2009; Bleakley and Hopkins, 2010; Costello et al., 2012b). Another important effect that WBC and PBC have shown in exercise recovery is an improvement in the quality of sleep (Bouzigon et al., 2014; Schaal et al., 2014). This effect may also be of importance to patients.

With the exception of 3 studies by Lubkowska et al. (2010, 2011, 2012) concerning the effects of 20 WBC exposures compared to 10 and 5 exposures, there have been no published studies regarding exposure protocols and the relationship between temperature, duration, number of repetitions and the treatments' desired effects.

Therefore, the aims of this review are to describe and compare the WBC and PBC technologies and to classify the protocols for exposure according to the desired effects. This study could provide methodological recommendations for health professionals.

A computer-based literature search was performed in March 2016 using the electronic databases PubMed and Science Direct to select relevant scientific articles. The selected studies were conducted over a 20-year period, up to and including January 2016. The key words used in the search were whole-body cryotherapy, whole-body cryostimulation, partial-body cryotherapy, partial-body cryostimulation, cryotherapy exposure, and extreme cold exposure.

Studies were eligible for inclusion if they were prospective, performed on humans and evaluated the effects of WBC and/or PBC. The research had to have been concerned with the effect of these procedures on skin and core temperature, psycho-physical health and post-exercise recovery. The studies had to be complete, include an abstract, and be written in English.

Table 2
Summary of the investigations on the effects of WBC and PBC on skin and core temperature.

Study	WBC or PBC, temperature measurement apparatus	Exposure temperature and duration	Measurement location	Mean skin temperature (°C)	Core temperature (°C)
Savic et al. (2013)	PBC Criomed Thermal camera	3 min −140 °C	Front and back: Chest, trunk and right and left upper arms, thighs and shank	Before: 32.7 °C After: 22.8 °C Variation: 9.9 °C	
Fonda et al. (2014)	PBC Criomed Thermolazer	1 min 30 s 2 min 2 min 30 s 3 min −140°C	Chest, arm, abdomen, thigh, calf	Variation: 1 min 30: 5.6 °C 2 min: 7.1 °C 2 min 30: 8.4 °C 3 min: 9.4 °C	
Hausswirth et al. (2013)	PBC Krion	3 min	Front side: Torso, abdominal, right and left: forearms, arms, thighs, and legs.	Before: 32.1 °C	Tympanic temperature Variation: 0.05 °C 20 min after the end of the exposure
	Thermal camera	−160 °C	Backside: Upper back, lower back, right and left: forearms, arms, thighs, and legs	After: 23.6 °C Variation: 8.5 °C	
Louis et al. (2015)	PBC Krion	3 min	Front side: Torso, abdominal, right and left: cheeks, forearms,	Variation: 1 exposure:	Tympanic temperature
	Thermal camera	−160 °C	arms, thighs, and legs	8.6 °C 5 exposures: 7.7 °C	Variation: 0.14 °C 20 min after the end of the exposure
Zalewski et al. (2013)	WBC Stan Mar three rooms: −10, −60 and −120 °C	3 min	Front side: Chest with shoulders, abdomen, right upper-arm, left upper-arm	Before: 31.7 °C After: 15.2 °C	
	Thermal camera	−120 °C	Backside: Upper back, lower back, right upper-arm, left upper-arm.	Variation: 16.5 °C	
Selfe et al. (2014)	WBC Juka two rooms: −60 and −135 °C Thermal camera	1 min 2 min 3 min −135 °C	Mean skin temperature	Variation: 1 min: 8.0 °C 2 min: 12.5 °C 3 min: 14.9 °C	Gastro intestinal temperature: No significant change
Cholewka et al. (2012)	WBC (Unknown model) two rooms −60 and −120 °C Thermal camera	3 min −120 °C	Front side: Head, chest, arms, tibias, hands, feet Backside: back	Before: 29.2 °C After: 23.4 °C Variation: 5.8 °C	Tympanic temperature Variation: 0.8 °C
Hausswirth et al. (2013)	WBC Zimmer three rooms:	3 min	Front side: Torso, abdominal, right and left: forearms, arms, thighs, and legs.	Before: 32.1 °C	Tympanic temperature Variation: 0.32 °C immediately after and 0.30 °C 20 min after the end of the exposure
	−10, −60 and −110 °C Thermal camera	−110 °C	Backside: Upper back, lower back, right and left: forearms, arms, thighs, and legs	After: 18.2 °C Variation: 13.9 °C	
Costello et al. (2012b)	WBC Zimmer two rooms −60 and −110°C Thermal camera	20 s −60 °C and 3 min 40 s −110 °C	Thigh	(Thigh) Before: 30.0 °C After: 18.0 °C Variation: 12.0 °C	Rectal temperature Variation: 0.25 °C 40 min after, 0.27 °C 50 min after and 0.30 °C 60 min after the end of the exposure
Costello et al. (2014)	WBC Zimmer two rooms −60 and −110°C Thermal camera	20 s −60 °C and 3 min 40 s −110 °C	Knees	Variation (knees): Right: 10.3 °C Left: 9.9 °C	
Westerlund et al. (2003)	WBC Zimmer three rooms: −10, −60 and −110°C Thermocouples	2 min −110 °C	Front side: Forehead, chest, arm, forearm, hand, thigh, upper foot. Backside: lower back, calf	Before: 32.0 °C After: 12.5 °C Variation: 19.5 °C	Rectal temperature No change during the first 30 min
Louis et al. (2015)	WBC Zimmer only room at −60°C used Thermal camera	3 min	Front side: Torso, abdominal, right and left: cheeks, forearms, arms, thighs, and legs	Variation: 1 exposure: 8.3 °C 5 exposures: 7.6 °C	Tympanic temperature Variation: 1 exp.: 0.28 °C 5 exp.: 0.34 °C
Hammond et al. (2014)	WBC (Unknown model) two rooms −60 and −110 °C Thermal camera	30 s −60 °C 2 min −110 °C	Chest, arm, thigh and calf	Variation: Females: 12.1 °C Males: 10.1 °C	-

(Abbreviations: WBC, whole-body cryotherapy; PBC, partial-body cryotherapy).

2. Whole- and partial-body cryotherapy technologies

2.1. Partial-body cryotherapy

PBC treatment is performed in a partial cryocabin called a cryo-sauna. It is an open tank in which the subject is exposed to cold, excluding the head and neck. This device was probably the first type of extreme cold technology for the body (Metzger et al., 2000). It was developed by Professor Yamauchi and was mentioned in the European Congress of Rheumatology in Wiesbaden, 1979 (Yamauchi, 1988). It was then further developed by Fricke (1989) in Germany and Zagrobelny et al. (1992) in Poland between 1980 and 1990. Cryo-saunas are less expensive to purchase than cryochambers, and they require less space, can be easily turned on and off and are transportable. This characteristic has recently allowed mobile PBC services to be present at sports events (e.g., the Tour de France, the Vuelta, and the European Basketball Championship). The limitations of this mobile device

Table 3
Summary of the investigations on the effects of WBC and PBC on physical and mental health.

Study	Disease	WBC or PBC treatment protocol	Modifications ('+': positive effect; '-': negative effect)
Gizinska et al. (2015)	RA	WBC (Unknown model) 10 exposures 1 per day/2 weeks 3 min −10 °C, −60 °C and −110 °C	+Inflammation +Pain +Fatigue +Disease score activity +Walking
Hirvonen et al. (2006)	RA	WBC (Unknown model) 20 exposures 3 per day/6 days and 2 the last day −60 °C −110 °C Unknown duration	+Pain (greater with −110 °C) +Morning stiffness +Disease score activity +Physician's global assessment
Jastrzabek et al. (2013)	RA	PBC (Unknown model) 20 exposures 2 per day/10 days 3 min −160 °C	+Decrease TNF-α +Disease score activity +Pain +Morning stiffness +Fatigue +Quality of life
Bettoni et al. (2013)	FM	WBC (Unknown model) 15 exposures 3 weeks 30 s at −60 °C and 3 min at −140 °C	+Pain +Fatigue +Disease score activity +Quality of life
Stanek et al. (2015)	AS	WBC Creator 10 consecutive days except weekend 30 s at −60 °C and 3 min at −120 °C	+Disease score index +Functional score index +Pain intensity +Spinal mobility parameters
Miller et al. (2016)	MS	WBC Kriosystem 10 exposures 3 min One per day / two weeks −60 °C and −110 °C to −160 °C	+Fatigue +Functional abilities
Miller et al. (2013)	MS	WBC (Unknown model) 10 exposures 3 min One per day/two weeks −130 °C	+Increase uric acid concentration in plasma +Improvement of the functional status
Miller et al. (2010)	MS	WBC (Unknown model) 10 exposures 3 min One per day/two weeks −60 °C and −110 °C to −160 °C	+Increase TAS +Increase superoxide dismutase -Decreased catalase
Nugraha et al. (2015)	Low back pain	WBC (Criomed) 10 exposures One per day 3 min at −5 °C or 3 min at −65 °C	+Pain +Disability index
Szczepanska-Gieracha et al. (2013)	Spinal pain syndromes Peripheral joint disease	WBC (Unknown model) 10 exposures 1 and 2 min for the two firsts exposures) 3 min the following eight sessions −60 °C and −130 °C	+General Well-being +Quality of life +Mood
Rymaszewska et al. (2008)	Depression and anxiety	WBC (Unknown model) 15 exposures 4 per week/1 per day 2 to 3 min −60 °C and −110 °C (first exposures) to −160 °C (lasts exposures)	+Depressive symptoms +Anxiety symptoms

(Abbreviations: WBC, whole-body cryotherapy; PBC, partial-body cryotherapy; RA, rheumatoid arthritis; FM, fibromyalgia; AS, ankylosing spondylitis; MS, multiple sclerosis; TNF-α, tumour necrosis factor alpha; TAS, total antioxidative status).

relate to the safety rules governing the transport and storage of nitrogen, which require the use of a second compartment (often a trailer) to transport the nitrogen tanks and the supply of nitrogen. Professional supervision is required for safe use of PBC, and appropriate safety procedures need to be applied.

PBC technology is based on direct contact between the patient and the nitrogen. Cold is created by spraying nitrogen directed at the body of the patient inside the tank. The patient's head must be out of the tank to prevent breathing nitrogen, which is an important safety problem. Nitrogen storage also involves regulatory issues. In France, it is not possible to store nitrogen tanks everywhere, and this can be a problem for both fixed and mobile devices. Centres with a fixed device must have a storage agreement, and it can be difficult to store nitrogen for mobile device services during field competitions.

Moreover, nitrogen is expensive, costing €20,000 to €30,000 per year for the Criomed and Juka models, and cryo-saunas consume large amounts of nitrogen. An advantage of PBC devices is they do not require much maintenance. According to the producing companies, the temperature of exposure in a cryo-sauna is between −110 °C to −195 °C, which is a rather wide temperature range. These temperature variations are due to the characteristics of nitrogen, which is stored in liquid form and gasifies at −195 °C. Therefore, the nitrogen sprayed inside the cryosauna during exposure is between −195 °C and −110 °C. Temperature adjustment is performed by spraying when the temperature inside the cabin rises above a certain level (e.g., above −115 °C if the selected temperature of exposure was −120 °C) at the site of the nitrogen

Table 4
Summary of the investigations on the effects of WBC and PBC on recovery enhancement after exercise.

Study	Outcomes/Subjects	WBC or PBC treatment protocol	Modifications ('+': positive effect; '-':negative effect; '=':no change)
Pournot et al. (2011)	Inflammation Trained runners 11 males	WBC Zimmer 4 exposures 1 per day 3 min −10 °C, −60 °C, −110 °C	Since first exposure: +Lower increase in IL-1β +Increase IL-1ra +Limited increase in CRP
Banfi et al. (2009)	Inflammation Elite rugby men 10 males	WBC (Unknown model) 5 exposures 1 per day 30 s −60 °C, 2 min −110 °C	+Increase IL-10 +Decrease IL-2 and IL-8 +Decrease sICAM-1 and PGE2
Lubkowska et al. (2011)	Inflammation Healthy men 45 males	WBC (Unknown model) 5, 10 and 20 exposures 1 per day 30 s −60°C, 2 min 30 s −110°C	+Increase IL-10 and IL-6 (higher with 20 exposures) + Decrease IL-1α
Ziemann et al. (2012)	Inflammation High rank tennis players 12 males	WBC (Unknown model) 10 exposures 2 per day 20–30 s at −60 °C, 3 min at −120 °C	+Decrease in TNF-α +Increase in IL-6
Ziemann et al. (2014)	Inflammation Physically active colleged-aged 9 males	WBC (Unknown model) 10 exposures 2 per day 20–30 s at −60 °C, 3 min at −120 °C	+Increase in IL-10 +Decrease in IL-1β +Decrease in muscular damage
Mila-Kierzenkowska et al. (2013)	Inflammation Professional volleyball players 18 males	WBC Metrum Cryoflex 1 exposure Before training 10–20 s at −60 °C 2 min at −130 °C	+Decrease in IL-6 +Limit the increase in IL-1β +Decrease in TNF-α
Ferreira-Junior et al. (2014a, 2014b)	Muscle damage Physically active participants 13 males	PBC Cryoness 1 exposure 3 min −110 °C	+Muscle strength +Pain =Muscle thickness
Hausswirth et al. (2011)	Muscle damage Train runners 9 Unknown gender	WBC Zimmer 3 exposures (1 h,24 h,48 h) 3 min in −110 °C room −10°C, −60°C, −110 °C	After the first exposure: +Maximal voluntary contraction +Perceived pain and well-being =Plasma CK activity
Fonda and Sarabon (2013)	Muscle damage Healthy men 11 males	PBC Criomed 6 exposures 1 per day/6 days 3 min −140 °C to −195 °C	+Pain +knee flexion rate of torque development +Squat jump start power +Maximal torque production =CK
Hausswirth et al. (2013)	ANS Healthy men 15 males WBC 15 males PBC	WBC Zimmer PBC Krion Standard 1 exposure 3 min −110 °C (WBC) −160 °C (PBC)	+Heart rate variability (HRV) indices
Schaal et al. (2013)	ANS Elite synchronised swimmers 11 females	WBC Zimmer 1 exposure 3 min in −110 °C room −10 °C, −60 °C, −110 °C	+HRV (RMSSD, HF band, SD1) +Maximal aerobic work output +Lactate variation +VO_{2peak} =Muscle pain =RPE =perceived effectiveness of recovery
Louis et al. (2015)	ANS Healthy men 10 males WBC 10 males PBC	WBC Zimmer PBC Krion Standard 1 exposure 3 min −60 °C (WBC) −160 °C (PBC)	+Catecholamines plasma concentration +HRV indices +ANS activity +Parasympathetic nervous system activity =Systolic and diastolic blood pressure
Westerlund et al. (2006)	ANS Healthy women 10 females	WBC Zimmer 1 to 36 exposures 2 min −10 °C, −60 °C, −110 °C	+HRV indices (RMSSD, SD1) =Attenuation of parasympathetic activity response after 3 months of repeated WBC
Schaal et al. (2014)	Sleep Elite synchronised swimmers 10 females	WBC Zimmer 14 exposures 3 min in −110 °C room −10 °C, −60 °C and −110 °C	+Get up time +Time in bed +Sleep latency and efficiency compared to control group +Perceived fatigue compared to control group

Table 4 (*continued*)

Study	Outcomes/Subjects	WBC or PBC treatment protocol	Modifications ('+': positive effect; '-':negative effect; '=':no change)
Bouzigon et al. (2014)	Sleep Elite basketball players 13 females 14 males	PBC Mecacel 1 exposure 3 min −130 °C	+Perceived quality of sleep =Cortisol
Wozniak et al. (2013)	Oxidative stress Elite rowers 6 Unknown gender	WBC kriotechnica Medyczyna KN-1 12 exposures 2 per day/6 days Before training 10–20 s at −60 °C 3 min at −125 °C to −150 °C	+Antioxidant activity +Lipid peroxidation products =CK
Mila-Kierzenkowska et al. (2009)	Oxidative stress Kayakers	WBC Metrum Cryoflex "Arctica" 1 exposure Before training 10–20 s at −60 °C 2 min at −130 °C	+Antioxidant activity +Markers of muscle damage and inflammatory
Sutkowy et al. (2014)	Oxidative stress Elite kayakers 9 women	WBC (Unknown model) 38 exposures 2 per day Before and after training 30 s at −60 °C 3 min at −120 °C	+Decrease in GPx +Decrease in TBARS

(Abbreviations: WBC, whole-body cryotherapy; PBC, partial-body cryotherapy; RA, rheumatoid arthritis; FM, fibromyalgia; AS, ankylosing spondylitis; MS, multiple sclerosis; TNF-α, tumour necrosis factor alpha; TAS, total antioxidative status; IL-1 α, interleukin 1 alpha; IL-1β, interleukin 1 beta; IL-1ra, interleukin 1 receptor antagonist; IL-2, interleukin 2; IL-6, interleukin 6; IL-8, interleukin 8; IL-10, interleukin 10; CRP, C-reactive protein; CK, creatine Kinase; RMSSD, root mean square standard deviation; HF, high frequency; SD1, standard deviation 1; RPE, rated perceived exertion; ANS, autonomic nervous system; HRV, heart rate variability; GPx, glutathione peroxidase; TBARS, Thiobarbituric acid reactive substances).

nozzle. The amplitude of the temperatures before and after adjustment may range from 10 to 20 °C, making it difficult to set and control precise temperatures. One study measured the exposure temperature in an empty cryo-sauna, the Criomed Model, with a manikin and with a participant during an exposure (Savic et al., 2013). In the empty cabin, the temperature next to the nitrogen nozzle dropped lower than −150 °C but stayed at −60 °C in the middle of the cabin. When a manikin was settled in the cabin, the temperature next to the manikin was not homogeneous. After 3 min (min) of exposure, the temperature was −100 °C at the top of the cabin and −140 °C at the lowest part of the cabin. The distribution of the temperatures was also different between the front and the back of the manikin. The mean temperatures measured next to the participant were between −20 °C for the chest and −40 °C for the shank, probably due to the participant's heat convection. On the body surface, an air layer called the boundary layer is created, which is a consequence of the convection. The authors speculated that the temperature is more constant in a cryochamber than in a cryo-cabin because the chamber is larger and contains a bigger volume of cold air, they also speculated that the greater number of nozzles on cryochambers play an important role. They showed that the actual temperature in the cryo-cabin was substantially different compared to the temperature reported by the cabin producer (Savic et al., 2013).

Studies have measured the variations in mean skin temperatures between pre and post-PBC exposure, and their findings have ranged from 5.6 °C (Fonda et al., 2014) (1 min 30 s, −140 °C, PBC Criomed, measured with a thermolaser) to 9.9 °C (Savic et al., 2013) (3 min, −140 °C, PBC Criomed, measured by thermal imaging). Fonda et al. (2014) have compared different PBC exposure durations using the Criomed Model ranging from −130 to −170 °C. The calculated variations in mean skin temperature were 5.6 °C for 1 min 30 s, 7.1 °C for 2 min, 8.4 °C for 2 min 30 s, and 9.4 °C for 3 min. Nevertheless, these data should be treated with caution because skin temperature was measured with a thermolaser. Thermolasers measure temperature at a specific point, and this measure is less sensitive than thermal imaging, which measures the temperature of the entire surface.

Hausswirth et al. (2013) measured the variations in tympanic temperatures (Krion Model, Saint Petersburg, Russia). They found minor changes 20 min after exposure (−0.05 °C). Louis et al. (2015) also showed reductions in tympanic temperature after PBC exposure with the same device of −0.28 °C after the first exposure, and of −0.34 °C after five exposures (one exposure per day). All the reported skin and core temperatures before, during and after PBC are presented in Table 2, with the device models used if they were described in the publication. PBC has been principally used in studies of exercise recovery. Only one study of rheumatoid arthritis patients has been performed with a PBC device (unknown model) (Jastrzabek et al., 2013).

2.2. Whole-body cryotherapy devices

The second type of devices is the whole-body cryochambers, in which the subject is entirely exposed to the treatment. These cryochambers are divided into two or three compartments of different temperatures, generally −10 °C, −60 °C and −110 °C to −160 °C. Chambers are often able to accommodate four or five individuals. There are two different ways to create cold air in the chambers. Chambers with large air compressors divide oxygen and nitrogen, and, once separated, the nitrogen cools. When it is sufficiently cooled, the nitrogen is remixed with oxygen (oxygen = 22 ± 2%) and injected into the chamber. The second type chamber creates cold by circulating nitrogen inside the compartment walls. This type of technology appears to be safer because the subject is not directly in contact with the nitrogen sprays. Nevertheless, it requires windows or a camera to observe the patient/subject, a security button to stop the treatment and a security door for fast exit. Again, professional supervision is required for safe use, and appropriate safety procedures must be applied.

In terms of mobility, no truly mobile WBC technology exists. One producer has developed a device in a container that can be

transported (WBC Kriosystem). However, the mobility of this container is limited because it requires a large truck for transport. A large truck is not suitable for following athletes at events (e.g., cycling races such as the Tour de France). The other WBC models take up a great deal of space and are not mobile. For example, the Zimmer devices consist of two parts, two or three chambers and the motor, which requires another entire room. The second mobility problem is the chamber's electrical supply: the chambers require a current of 380 V, and the necessary jacks are not common. However, there are some newer products for which 240 V is sufficient. WBC devices are more expensive to purchase than PBC devices (€80,000 to €350,000 and €45,000 to €60,000, respectively). WBC devices also require important maintenance.

Studies have measured the variations in mean skin temperatures between pre- and post-exposure in WBC devices, and their findings have ranged from 5.8 °C (Cholewka et al., 2012) (3 min, −120 °C, unknown model, measured by thermal imaging) to 19.5 °C (Westerlund et al., 2003) (2 min, −110 °C, WBC Zimmer, measured with thermocouples). This second result should be viewed with caution because the lowest temperature was measured during exposure, and the measurements were performed using thermocouples. Thermocouples record temperature at a specific point, and the recorded temperature may easily have been affected by different factors during the exposure. Thermocouples also have other shortcomings. Nevertheless, the primary goal of this study was to ensure that a 2 min WBC exposure at −110 °C involved no risk of frostbite. Such an approach should be required when different exposure durations and temperatures are used. Another interesting finding of this study was the notable increase in skin temperature immediately after exposure. The study's results showed that measurements of skin temperature must be performed quickly after exposure to obtain the actual lowest skin temperature.

One study compared the effect of several WBC exposure durations on the skin temperatures of fourteen professional rugby players (Selfe et al., 2014). These findings showed that the most significant decrease in mean skin temperature occurred during a 3 min WBC exposure period (14.9 °C) rather than a 2 min (12.5 °C) or 1 min exposure period (8 °C). Hammond et al. (2014) compared skin temperature variations between females and males after a WBC exposure of 60 s at −60 °C and 2 min at −110 °C. The findings showed a greater decrease of temperature in females (12.7 °C) than in males (10.1 °C).

The effect of WBC on core temperature has been measured in several studies. Two studies reported no change in the first 30 min post-exposure for gastro intestinal (Selfe et al., 2014) and tympanic (Westerlund et al., 2003) temperatures. Three other studies demonstrated significant decreases in tympanic temperature (Cholewka et al., 2012; Hausswirth et al., 2013; Louis et al., 2015) and one study showed a significant decrease in rectal temperature (Table 2). All the reported skin and core temperature values and variations before and after WBC are shown in Table 2; the models of the devices that were used are provided when known.

Costello et al. (2012b) measured the decrease in muscular temperatures of the vastus lateralis at a depth of 1, 2 and 3 cm after a 4-min WBC exposure (30 s at −60 °C and 3 min 30 at −110 °C; WBC Zimmer, measured with a flexible intramuscular temperature probe). The authors reported significant decreases in muscular temperature 1 h after exposure for the three depths (1 cm: −1.6 °C; 2 cm: −1.2 °C; 3 cm: −1.6 °C) and a significant effect over time in deep muscle temperature (3 cm subcutaneous) compared to baseline (from −0.9 °C post 20 min to −1.7 °C post 60 min).

WBC has been used in studies measuring the effects of cryotherapy on physical and mental health and on post-exercise recovery.

2.3. Advantages and limits

PBC appears to have the most advantages in the sport recovery domain, especially when the treatment must be performed in the field. PBC devices are mobile, require less space and can easily be turned on and off. WBC devices require more space and are not mobile. However, a significant number of the available of this technology have demonstrated that WBC confers benefits in most domains. Moreover, WBC appears to induce greater mean skin temperature and core temperature variations pre- and post-exposure than PBC. WBC devices enable the treatment of several patients at the same time, and this could be important in the sport recovery domain by allowing athletes to spend less time waiting for treatment exposure during competitions days.

The first limitation of these two technologies is safety, particularly for the PBC. However, although PBC devices may be more dangerous because patients are in direct contact with nitrogen, it is easier to exit a PBC cabin. Individuals are entirely exposed in WBC chambers, and the devices require a way to communicate visually and orally with the individuals. Moreover, there must be emergency stop buttons and exits. The second limitation is energy consumption. PBC devices are less expensive to purchase; however, they are large consumers of nitrogen, and nitrogen is expensive. Furthermore, during competition services, nitrogen is not easy to supply. The electrical supply for WBC devices is also of importance and typically requires a 380 V of current. WBC chambers also require more maintenance than PBC cabins. The third limitation is the heterogeneity of the temperature during exposure in a PBC device. No data are available concerning the temperatures inside WBC chambers. Finally, the last limitation is the place of installation. PBC devices are mobile, but the regulations for nitrogen storage are restrictive. It is not possible to store nitrogen everywhere. WBC devices have fewer regulation problems and no nitrogen storage problems, but they require a great deal of space.

After reviewing studies of cryotherapy/cryostimulation, it appears that a great deal of information is lacking regarding the technology used (model, origin, etc.) and precise temperatures during exposure. The diversity of the technologies used in the studies also raises the question: What are the optimal exposure temperatures required to achieve the desired effects? Finally, the actual temperatures of exposure in both devices remain unknown. The only available study results that are relevant to this context showed a temperature of approximately −50 °C rather than the expected −110 °C.

3. Whole- and partial-body cryotherapy exposure protocols

3.1. Application in the physical and quality of life domains

3.1.1. Rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic, autoimmune, inflammatory and destructive joint disease. Patient mobility is decreased due to chronic pain and morning stiffness, and functional disability affects the quality of life of the patient (Aletaha et al., 2010). Pro-inflammatory cytokines, especially interleukin-6 (IL-6) and tumour necrosis factor-α (TNF-α) play key roles in local and systemic manifestations of RA, inducing fatigue, pain and depression (Choy, 2012).

WBC use has induced positive effects in patients with RA. During a 2-week rehabilitation program, a significant reduction in IL-6 and TNF-α was shown in 25 patients with RA after WBC treatment (Gizinska et al., 2015). The treatment protocol was ten 3-min exposures at −110 °C. Patients performed one daily exposure for the two-week period, excluding weekends. In addition

to a decrease of pro-inflammatory cytokine concentrations in the blood, the authors demonstrated an improvement in pain and fatigue status according to a visual analogue scale (VAS) and disease activity score 28 (DAS28), which considered the number of swollen and tender joints, global VAS score as assessed by the patient, and the erythrocyte sedimentation rate. Finally, walking time and the numbers of steps taken in a walking test of 50 m decreased. Jastrzabek et al. (2013) found similar results in a study of 40 RA patients. They also demonstrated a decrease in the concentration of circulating TNF-α after treatment. The study protocol consisted of twenty 3-min PBC sessions at −160 °C conducted twice daily for ten days.

Another study of 40 patients with RA showed a decrease in pain sensation and morning stiffness on the VAS and in disease score activity (DAS28) and an improvement in the physician's global assessment (Hirvonen et al., 2006). The protocol consisted of twenty exposures, three daily for six days and two on the last day. Two exposure temperatures were compared: −60 °C and −110 °C. The duration of exposure was not indicated. The patients were randomized between the two groups (20 per group). Between the groups, the −110 °C WBC group showed a greater decrease in pain than the −60 °C WBC group.

A recent meta-analysis of six studies and 257 RA patients showed that consistent use of WBC (14–20 applications) significantly decreased pain on the VAS and DAS 28 (Guillot et al., 2014). It appeared that the repetition of exposure was significant in treatment efficiency.

3.1.2. Fibromyalgia

Fibromyalgia is a chronic widespread pain disorder. The allodynia and hyperalgesia induced by an imbalance in the level of the neurotransmitters and in pro- and anti-inflammatory mediators are the sources of neurological pain. Fibromyalgia involves fatigue, sleep problems and other frequent comorbid physical and mental disorders (Trinanes et al., 2014).

A study has already demonstrated that patients with fibromyalgia (FM) treated with WBC report an improvement in quality of life (Bettoni et al., 2013). This study was conducted with 50 patients with FM. The WBC treatment protocol consisted of 15 sessions over a period of 3 weeks. Each session duration was 30 s at −60 °C and 3 min at −140 °C. In this study, a VAS was used to measure pain and a self-assessment questionnaire regarding global health status was used to calculate the disease activity score. A qualitative score of the physical and mental health of the patients with FM was obtained via the Short Form Health Survey (SF-36). Fatigue was evaluated with the Fatigue Severity Scale. The findings showed a positive effect of WBC on the quality of life of a group of patients with FM as demonstrated by improvements in all the qualitative indexes. The authors speculated that improvement was due to the effects of cryotherapy on the balance between pro- and anti-inflammatory mediators, which have a role in the modulation of pain (Lubkowska et al., 2010, 2011; Bettoni et al., 2013).

3.1.3. Ankylosing spondylitis

Ankylosing spondylitis (AS) is a chronic, usually progressive inflammatory rheumatic disease affecting primarily the axial skeleton and sacroiliac joints. Chronic inflammation in the spine can develop into a complete fusion of the vertebrae. This phenomenon is called ankylosis, which causes a total loss of mobility of the spine. Moreover, AS may affect peripheral joints, skin, eyes, bowels or lungs (Stanek et al., 2015). The symptoms of the disease include pain and stiffness in the lower back, the upper buttock area, the neck, and the remaining regions of the spine, which may lead to structural and functional impairment (Gran and Skomsvoll, 1997).

A study of 48 males demonstrated the positive effects of WBC treatment in AS patients. The participants were divided into two groups (Stanek et al., 2015). A group of 32 patients were exposed to WBC procedures with subsequent kinesiotherapy and a group of 16 patients were exposed only to the kinesiotherapy procedure. The WBC protocol was ten 3-min exposure sessions, once a day for 10 consecutive days, excluding the weekend. The exposure times and temperatures were 30 s in a −60 °C chamber and 3 min in a −120 °C chamber. Immediately after leaving the cryotherapy chamber, patients in the WBC group underwent a one-hour kinesiotherapy session. The primary outcomes consisted of the measure of two indexes, the BASDAI and the BASFI. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) includes six questions related to fatigue, back pain, peripheral pain and swelling, local tenderness and morning stiffness (degree and length). The Bath Ankylosing Spondylitis Functional Index (BASFI) is the mean score of ten questions addressing functional limitations and levels of physical activity at home and work assessed on VAS scales (0=easy; 10=impossible). The secondary outcomes consisted of pain intensity and chosen spine mobility parameters. After the completion of the treatment, all measured parameters were improved in both groups. The examined parameters' changes were significantly higher in the WBC group than in the kinesiotherapy group. The authors observed a decrease of approximately 43% of pain intensity in the WBC group. The BASDAI estimates the disease score activity. In this study, disease scores decreased approximately 40% in the WBC group. Moreover, after the completion of the treatment, the WBC group's score value corresponded to an “inactive disease” score. The same conclusion was reached using the BASFI, which showed a decrease in pain of approximately 30% in the WBC group, with a corresponding score of “inactive disease”. This study demonstrated that WBC treatment has positive effects on AS patients in terms of disease and functional score indexes, in the reduction of pain intensity and in the improvement of some spinal mobility parameters.

3.1.4. Multiple sclerosis

Multiple sclerosis (MS) is a chronic heterogeneous disease with an unpredictable clinical course. Symptoms can include paralysis, ataxia, spasticity, incontinence, and fatigue syndrome. Fatigue is considered to be the most prevalent and disabling of the symptoms at all stages of the illness, and it occurs in 70–80% of patients. This characteristic of the disease directly impacts the quality of life of patients, affecting their social, physical and occupational well-being (Miller, 2012). Heat stress also presents a problem in MS patients. It appears that a decrease in body temperature might increase the conduction of nerve signalling and alleviate many symptoms, particularly fatigue (Miller, 2012).

A recent study showed an improvement in the fatigue status and functional abilities of MS patients who had ten 3-min WBC exposures between −110 °C and −130 °C (Miller et al., 2016). The patients received one exposure each day for two weeks, excluding the weekend. Miller et al. (2010, 2013) also showed a long-lasting effect on the level of uric acid, the main antioxidant in human blood, in 22 MS patients who had ten 3-min exposures at −130 °C. Extended disability status was assessed using a perceptive scale, and the findings showed a decrease in disability with WBC treatment. Miller et al. (2010) also showed an increase in total antioxidative status levels in the plasma of 22 MS patients who received between 2 and 3 min of WBC exposure at −160 °C. Moreover, the effect was greater in depressive MS patients (n=12) than in non-depressive MS patients (n=10).

3.1.5. Chronic low back pain

Chronic low back pain is one of the most frequent musculoskeletal pain syndromes. Acute low back pain is self-limiting and becomes a chronic pain syndrome that has an important impact

on quality of life. In one study, demonstrated pain relief in patients who suffered from low back pain was shown using three different perceptual scales (Nugraha et al., 2015). Interestingly, this study showed the same effect from ten 3-min WBC exposures (one per day) at −65 °C and at −5 °C in a cryochamber for this pathology.

Previous studies have shown that local analgesia in cryotherapy requires the skin temperature to be below 13.6 °C, when nerve conduction and acetylcholine formation become suppressed (Bugaj, 1975). In most of the studies mentioned in the first paragraph, this temperature was not reached. Nevertheless, pain was found to be alleviated, although skin temperatures remained well above 13.6 °C. Nevertheless, this temperature can be reached in the back during the exposure (Leppaluoto et al., 2008). According to Leppaluoto et al. (2008), pain alleviation can be explained by a lessening of nerve transmissions over a large area of the body, and it is also possible that humoral mechanisms may be responsible for alleviating symptoms after whole-body cryotherapy.

3.1.6. Depression and anxiety symptoms

The impact of WBC on well-being, mental state and quality of life has not been the subject of many scientific studies. The few investigations of these topics have been conducted with patients suffering from depressive symptoms, anxiety, spinal pain syndromes or peripheral joint disease. The main outcomes were assessed using perceptual scales or surveys. WBC has a beneficial effect on patient quality of life because patients experience a decrease in pain (cf. paragraph II). Such a change may be linked to hormonal responses. Indeed, WBC increases body metabolism and the plasma concentrations of catecholamine (adrenaline, noradrenaline), cortisol, adrenocorticotropic hormone (ACTH) and β-endorphins (Leppaluoto et al., 2008). However, the increase of plasma ACTH, cortisol and β-endorphins was lower after several exposures. In contrast, there was no habituation for the increase in noradrenaline.

Depression may be due to neurobiological dysfunction with a dysregulation of the hypothalamic-pituitary-adrenal axis. The brain's opioid peptide systems are known to play an important role in motivation, emotion, attachment behaviour, response to stress and pain, and the control of food intake (Nestler et al., 2002). It appears that the positive effects of WBC on both external and internal pain are due to the activation of the endogenous opioid system and “pain control system”. This multi-system reaction could play a role in the treatment of mental disorders (Rymaszewska et al., 2008).

Studies have demonstrated that general well-being, quality of life and mood were improved in patients with spinal pain syndromes or peripheral joint disease who received ten 3-min WBC exposures (Szczepanska-Gieracha et al., 2013). Depressive symptoms, anxiety, and other mental states were also improved by the therapy. Moreover, this study showed that the strongest effects were noted in patients with the greatest problems in terms of mood and well-being before beginning the therapy. Rymaszewska et al. (2008) showed positive effects after one week of treatment (5 exposures) in 26 patients with depressive and anxiety disorders. The improvements continued to be significant over the entire three-week cycle of cryotherapy, with 15 exposures of 2–3 min at temperatures ranging from −110 °C for the first session to −160 °C for the last session.

3.1.7. In summary

According to the literature, WBC and PBC have positive effects on the physical and psychological parameters of RA patients, and WBC has positive effects on the physical and psychological parameters of patients with FM, AS and MS. It appears that the WBC and PBC exposure protocols for these types of pathologies must include at least ten 3-min WBC exposures, one per day. The minimum necessary exposure temperature is −60 °C, although a colder temperature induces greater effects (Table 3).

- Ten to twenty 3-min WBC or PBC exposures, one per day, between −60 °C and −110 °C appears to be effective for RA patients.
- Fifteen 3-min exposures, one per day, at −140 °C appears to be effective for FM patients.
- Ten WBC exposures, 30 s at −60 °C and 3 min at −120 °C, one per day, appears to be effective for AS patients.
- Ten 3-min WBC exposures between −120 °C to −130 °C, one per day, appears to be effective for MS patients.
- Ten 3-min exposures at −5 °C or −65 °C, one per day, appears to be effective for low back pain patients.

WBC also appears to have positive effects on mental state and well-being in several patient groups. Studies have demonstrated the benefits of several 2- or 3-min exposures from −110 °C to −160 °C (Table 3).

- Ten 3-min WBC exposures, with 1- and 2-min exposures for the first two sessions at −130 °C, are recommended for patients with spinal pain syndromes and peripheral joint disease.
- Fifteen 2- or 3-min WBC exposures, one per day, four per week, from −110 °C to −160 °C are recommended for patients with depressive or anxiety syndromes.

3.2. Application in physical exercise recovery

3.2.1. Inflammatory response

Intense training can induce muscle damage and subsequent inflammation. Muscle soreness, swelling and prolonged loss of muscle function can follow exercise. Strenuous exercise induces the release of the C-reactive protein (CRP) and an increase in the pro-inflammatory cytokines TNF-α, IL-1β, IL-2 and IL-8 and in the myokine IL-6 in the circulatory system. In response to this phenomenon, there is a release in the interleukin inhibitor interleukin 1 receptor antagonist (IL1-ra) and in the anti-inflammatory cytokine IL-10 (Chatzinikolaou et al., 2010; Ostrowski et al., 1999).

WBC is used to limit the inflammatory process that occurs subsequent to physical exercise. A study showed the positive effects of WBC on recovery after a single bout of running exercise. Eleven well-trained runners performed a 48-min simulated training race with different intensities, which was followed by WBC (Pournot et al., 2011). The protocol consisted of 4 sessions of 3 min at −110 °C after crossing through the chambers at −10 °C and −60 °C. The sessions were performed immediately and 24 h, 48 h and 72 h after the simulated run. The study found that a single exposure to WBC significantly alleviated inflammation after the run. Compared to a passive condition, the study observed a lower increase in IL-1β 1 h after exercise, a greater increase in IL-1ra 1 h and 24 h after exercise, and a strongly limited increase of the CRP at 24 h up until 48 h after exercise. The authors concluded that a single session of WBC exposure for 3-min at −110 °C performed immediately after exercise enhanced muscular recovery by restricting the inflammatory process due to exercise-induced low to moderate muscle damage.

A study of ten professional rugby players demonstrated an increase in the concentration of anti-inflammatory cytokine IL-10, and decreases in pro-inflammatory cytokine IL-2, chemokine IL-8, the level of soluble intercellular adhesion molecules 1 (sICAM-1) and prostaglandin. The players had to perform 5 WBC sessions, one per day, after 3 h of training. They were exposed at −60 °C for 30 s and at −110 °C for 2 min (Banfi et al., 2009).

Lubkowska et al. compared the effects of several repetition protocols (one per day) for WBC exposure on inflammatory

parameters (Lubkowska et al., 2011). The participants consisted of 45 healthy subjects divided into three equal groups. One group received WBC once a day for 5 consecutive days; the second group had 10 daily WBC exposures for two weeks, excluding the weekend; and the third group received 20 WBC exposures, once a day for four weeks, excluding weekends. Each WBC session lasted 3 min, 30 s at −60 °C and then 2 min 30 s at −130 °C. Several participants occupied the chamber at the same time. The levels of myokine IL-6 and anti-inflammatory cytokine IL-10 increased after 5, 10 and 20 WBC exposures, returning to the initial state two weeks after exposure. The most significant increase was observed with 20 exposures. The level of pro-inflammatory cytokine IL-1α decreased with the three treatments and remained decreased two weeks after the series of 20 exposures. The authors suggest that a series of 20 exposures conveys higher anti-inflammatory effects.

Ziemann et al. (2012) showed that the use of WBC for 5 days combined with moderate-intensity training was more effective for the recovery process, especially for decreasing inflammatory syndrome after exercise, than the training alone. Indeed, at the end of a five-day training camp, the authors observed an improvement in the cytokine profiles of twelve professional tennis players who were exposed to WBC after training. The players had to perform ten 3-min WBC exposures at −120 °C twice a day for five days. A decrease in TNF-α and an increase in IL-6 were observed. Similar findings were found in 9 healthy active men (Ferreira-Junior et al., 2014b). These subjects performed eccentric exercises to induce muscle damage and then rested for five days, during which they had two 3-min WBC sessions at −110 °C each day. They then performed a second round of eccentric exercise, and the study showed that the five days of rest accompanied by WBC significantly enhanced the concentration of the anti-inflammatory cytokine IL-10, significantly reduced the level of pro inflammatory cytokine IL-1β and reduced muscle damage. Moreover, after the second round of exercise, the concentration of IL-10 was two-fold higher in comparison to the baseline, whereas the concentration in the control group remained unchanged.

Mila-Kierzenkowska et al. (2013) showed that WBC exposure (2 min at −130 °C) before a submaximal exercise limited inflammation after exercise in 18 professional volleyball players, compared to a control group that did not receive WBC.

3.2.2. Muscle damage recovery

An unusual and/or high-intensity physical exercise can induce delayed-onset muscle soreness, resulting in a sensation of discomfort, predominantly within the skeletal muscles. Muscular performance may temporarily be impaired for several minutes, hours or days following very intense exercise. This may interfere with athletic training or competition (Costello et al., 2012a).

Some studies have investigated the effects of WBC and PBC on muscle damage recovery. A study of 26 physically active males demonstrated faster recovery of muscle strength and relieved pain 72 h after damaging exercises (five sets of twenty drop jumps from a 0.6 m box) with no alteration in muscle thickness one 3-min PBC exposure at −110 °C was used 10 min after the exercise in comparison with a control group (Ferreira-Junior et al., 2014b). Hausswirth et al. (2011) assessed the effects of three WBC exposures at 1 h, 24 h and 48 h after a damaging simulated trail run in nine highly-trained endurance runners. They demonstrated that maximal muscle strength and perceived sensations (pain and well-being) were recovered after the first WBC session (post 1 h) while recovery took 24 h when using a passive recovery method. The participants using WBC traversed two rooms at −10 °C and −60 °C and stayed at −110 °C for 3 min

Improvements in pain, knee flexion, rates of torque development, start squat jump power and maximal torque protection were in eleven healthy males with PBC exposure after plyometric exercise (Fonda and Sarabon, 2013). Subjects performed six PBC exposures, one per day, for six consecutive days after the plyometric exercise (the first exposure was organised 1 h after the end of the exercise). The protocol was a 3-min exposure at −140 °C to −195 °C. Pain sensation was lower in the treatment group than in the control group from the first exposure to the fourth (post 72 h). Squat jump start power was higher for the treatment group than the control group after the first exposure, while maximal torque production and torque rate of development were better after the second exposure (post 24 h).

These articles demonstrate the beneficial effects of WBC and PBC on pain and well-being sensations and on muscle strength recovery after exercise-induced muscle damage resulting from moderate (trail run) and high intensity (plyometric) exercise. Nevertheless, two WBC exposures two hours apart for 3 min at −110 °C performed 24 h after the muscle-damaging exercise were not able to improve muscle soreness or force recovery (Costello et al., 2012a). These findings were probably due to the time between exercise and WBC exposure and the physical activity level of the participants. The subjects were not very physically active and the exercise-induced damage may have been too great. In this study, the physical exercise was only eccentric; whereas in the other studies, the physical exertion was a combination of concentric and eccentric exercises, which induced a lower level of muscular damage. WBC and PBC may have positive effects on muscle pain and strength recovery, but to obtain these benefits muscular damage should not be too extensive, and exposure should be performed in the first few hours after exercise.

3.2.3. Autonomic nervous system

The autonomic nervous system (ANS) influences the modulation of cardiac activity. At rest, the two branches of the ANS establish an equilibrium for the heart rate. The sympathetic branch accelerates the heart rate through neural and humoral pathways (catecholamine), while the parasympathetic branch decelerates the heart rate through neural pathways. Parasympathetic activity is known to be related to exercise recovery and to a decreased risk of cardiovascular incidents (Bieuzen et al., 2015).

Another study further demonstrated increased ANS activity, predominantly of the parasympathetic branch, after a single exposure of WBC and PBC (Hausswirth et al., 2013). The study involved 40 healthy men who received a single 3-min WBC exposure at −110 °C and a single 3-min PBC exposure at −160 °C. The results showed that WBC had a greater effect on ANS. According to the authors, head exposure to the cold accentuates parasympathetic activation by cold stimulation in the trigeminal brain stem. However, another study showed less variation in the effects of these two methods on ANS (Louis et al., 2015). The authors compared the effects of PBC at −160 °C and WBC at −60 °C. Plasma norepinephrine concentration after the first exposure was similar for both techniques. However, this study evaluated WBC exposures at −60 °C, and the authors reported that plasma catecholamine concentrations and ANS activity responses were lower at this temperature than in studies with WBC exposure at −110 °C.

A study of eleven elite synchronised swimmers also reported an increase in heart rate variability indices reflecting parasympathetic activity with a single 3-min WBC exposure at −110 °C conducted after ballet training (Schaal et al., 2013). The authors also observed a larger clearance of plasma lactate. The swimmers reached higher VO2 peak values in the second exercises when they received a WBC exposure after the first exercise. It was interesting to observe the strong influence of a single WBC exposure received shortly after a maximal exercise on parasympathetic reactivation in this study.

Westerlund et al. (2006) also showed an increase in

parasympathetic activity in ten females who were moderately physically active after a single 2-min WBC exposure at −110 °C. However, when such exposures were repeated over 3 months with 3 exposures per week, an attenuation in the increase of the parasympathetic tone was observed. It would be interesting to investigate this "cold habituation" finding in a study on exercise recovery.

3.2.4. Quality of sleep

The quality of sleep is considered key to the recovery process of athletes (Samuels, 2008). Two studies have recently demonstrated the beneficial effect of WBC and PBC on sleep quality. The first study investigated the effects of fourteen 3-min WBC exposures at −110 °C (one per day for fourteen consecutive days) in ten elite synchronised swimmers during an intense training period (experiment leading to a functional overreaching in athletes) (Schaal et al., 2014). The authors demonstrated the positive effects of the treatment on sleep latency and efficiency and perceived fatigue compared to the control group. The second study, conducted during international competitions, showed a 15% enhancement in perceived sleep quality in 27 elite basketball players after a single 3-min PBC exposure at −130 °C (Bouzigon et al., 2014).

3.2.5. Oxidative stress

The cells continuously produce free radicals and reactive oxygen species (ROS) as part of the metabolic process. These free radicals are neutralised by elaborate antioxidant defence systems consisting of enzymes such as superoxide dismutase, catalase and glutathione peroxidase and numerous non-enzymatic antioxidants (Stankovic and Radovanovic, 2012). Physical exercise induces an enhanced formation of ROS, which is closely correlated with muscle action intensity. The imbalance between ROS and antioxidants is called oxidative stress. If the increase in free radicals is greater than the ability to neutralise them, the radicals will attack cellular components, especially lipids. This phenomenon is called lipid peroxidation and leads to the generation of more radicals and ROS that can harm other cellular components and induce membrane damage (Urso and Clarkson, 2003). A pioneering study in winter swimmers has shown that repeated extreme cold exposure induces significant oxidative stress (Siems and Brenke, 1992). These results have since been counterbalanced, and several studies have shown that acute and regular WBC and winter swimming lead to an increase in plasma antioxidative capacity (a protective effect). A series of thirty-six 2-min WBC exposures at −110 °C during a period of 12 weeks or after winter swimming sessions (Dugue et al., 2005), as well as a series of twenty 3-min WBC exposures at −130 °C were able to increase plasma antioxidative capacity (Lubkowska et al., 2012).Lubkowska et al. (2008, 2009) suggested that one-time WBC is a stress-inducing factor for a healthy body with a low level of oxidative stress and that a repetition of exposures may lead to the activation of antioxidant defence mechanisms in the body. The authors demonstrated that a single session of 3-min WBC exposure at −130 °C was able to significantly lower the level of plasma total oxidative status 30 min after the end of the exposure. This level remained low the following day, whereas the level of total antioxidative status decreased after cold exposure and increased the following day. The same observation was found in a study of obese participants (Lubkowska et al., 2015). The study demonstrated that two treatments of 20 daily WBC exposures before and after six months of moderate aerobic activity resulted in an increase in the activity of the anti-oxidant enzyme superoxide dismutase in the period following the WBC exposure.

The use of WBC prior to training may reduce the risk of oxidative stress and the extent of muscle fibre injuries provoked by intense exercise (Wozniak et al., 2013). These effects were demonstrated in a study on six elite rowers. Two daily WBC sessions before trainings were organised over 6 days. The exposure protocol was 10–20 s at −60 °C and 3-min from −125 °C to −150 °C. The activity of superoxide dismutase and glutathione peroxidase in blood was lower after the third day of training in the subjects who received WBC than in the subjects who were not exposed to WBC. WBC exposure before the training also led to a decrease in circulating peroxidation products in elite rowers, whereas the training alone led to an increase in the concentration of those products.

The same findings were observed in a study of eighteen male professional volleyball players (Mila-Kierzenkowska et al., 2013). The players experienced one 2-min WBC exposure before a 40-min sub-maximal exercise period on a cycle ergometer. The activity of superoxide dismutase and catalase were lower after exercise preceded by WBC. The study also found a lower concentration of the pro-inflammatory cytokine IL-1β after exercise preceded by WBC. The protocol was a single 2-min exposure at −130 °C after 10–20 s at −60 °C.

Sutkowy et al. (2014) showed a decrease in oxidative stress in 16 international level kayakers who combined WBC with their training during preparation for the world championship. The athletes received two exposures per day, before and after training, for 19 days. They were exposed for 30 s at −60 °C and 3 min at −120 °C. After 5 days, a decrease in glutathione peroxidase (GPx) occurred. However, after 19 days, there was a decrease in thiobarbituric acid reactive substances (T-BARS), indicating a decrease in lipid peroxidation.

3.2.6. In summary

Current literature suggests that single and repeated short-term treatments with WBC or PBC after exercise have beneficial effects on exercise recovery (Table 4).

- A decrease in the inflammatory process seems to occur with a single 2- or 3-min WBC exposure at −110 °C after exercise. A 2-min WBC exposure at −130 °C before submaximal exercise also resulted in a decrease in the inflammatory response after exercise.
- Relief of exercise-induced muscular pain is obtained from one to six 3-min PBC or WBC exposures. The exposure temperatures can range between −110 °C and −195 °C. However, the muscular damage must not be too extensive, and the exposure must occur less than 24 h after the end of the exercise.
- Improvement in ANS activity, especially parasympathetic post-exercise reactivation, is shown to occur after the first cold exposure and through a series of 38 exposures (two per day, before and after training). However, with prolonged treatment, the parasympathetic activity response is attenuated. The exposure can be conducted with either PBC or WBC. The protocol for WBC should be a 2- or 3-min exposure from −60 °C to −110 °C; the protocol for PBC should be a 3-min exposure at −160 °C.
- Enhancement of the quality of sleep was observed after a single 3-min PBC exposure at −130 °C and after fourteen 3-min WBC exposures at −110 °C (one exposure per day).
- Finally, WBC exposure before exercise reduces exercise-induced oxidative stress. This effect occurs after only one exposure. The duration can be a 2-min exposure at −130 °C or a 3-min exposure between −125 °C and −150 °C.

3.3. Advantages and limits

It appears that WBC and the PBC have significant positive effects in several domains. Furthermore, no negative effects on the studied parameters were found. While several studies reported no effect, none of them reported negative effects.

The current problems in need of resolution include the absence of standardisation in PBC and WBC protocols. Studies showed the beneficial effect of PBC and WBC, but the protocols were often different, especially in terms of exposure temperature. This may be explained by the differences between the technologies used of the two treatments and by the differences among the devices used in the studies. It is of primary importance to determine the validity and practicality of the two technologies. Additionally, the exposure temperatures inside each PBC and WBC model should be measured with a higher degree of precision.

The same cold stimulus at the same temperature for the same duration may be perceived differently by different subjects. Anthropometric characteristics, especially body mass index (BMI), are known to influence thermal transfer in humans subjected to cold stimuli (Dugue and Leppanen, 2000; Glickman-Weiss et al., 1993; Parsons, 2002; Smolander et al., 2004). Moreover, it appears that gender may also have an influence. Therefore, it would be of interest to consider the anthropometric and gender characteristics of patients/subjects to determine individualised exposure protocols (duration and temperature). This methodological paragraph also highlights the small number of PBC studies and the lack of comparisons among temperatures regarding cold-induced effects (e.g., the effects of WBC at −110 °C vs WBC at −130 °C).

More extensive investigations over longer periods of time are needed to study the long-term effects of WBC and PBC on health outcomes. Although several studies assessed the effects of multiple exposure treatments, the longest duration of assessment was three months (Dugue et al., 2005; Miller et al., 2013). Consequently, there is no data available regarding the effects of WBC and PBC beyond three months of treatment. Additionally, data should be collected at intervals after the end of the WBC/PBC series of exposures to learn whether the cold-induced benefits are kept.

4. Conclusions and perspectives

WBC and PBC are experiencing considerable development in several domains. The two treatments have become a common topic in the areas of health, sport and well-being. Additionally, an increasing number of scientific articles have reported the effects of these therapies. It was therefore necessary to take stock of the technological and scientific evolution of these treatments. This review demonstrated the lack of information regarding actual temperatures inside the cabin or chamber during exposure. Currently, the temperature provided by the WBC device producers is −110 °C, but it is very difficult to verify this temperature without data. The only measurement performed during an exposure showed a temperature of approximately −50 °C in the centre of a cabin without a participant inside (Savic et al., 2013). Indeed, it appears that the technologies used are not able to effectively control the temperature inside the cabins and chambers. More elaborate future systems should help to optimize treatment protocols by offering a more precise temperature control inside the room and a better distribution of cold.

This review also demonstrated the heterogeneity among the exposure protocols used in the scientific literature. To develop a truly effective repertoire of exposure protocols, a method should be established to measure the temperatures in all of the WBC and PBC models. Additionally, the wide variety of protocols in place across the different exposure times will certainly require more methodological relevance. It would be interesting to more precisely study the effects of different temperature, and the duration and the number of exposures. The anthropometric characteristics and gender of the patient should consider. Additionally, improved precision would allow observation of the dose-response effect of different exposure protocols. The accumulation of data would lead to optimisation of WBC and PBC exposure protocols, which would serve the function of achieving the desired effect according to each individual's needs.

Technologically, it is imperative to develop a safe device for the patient. Indeed, Table 1 shows that there is a lack of information relating to the European community medical marking (CE Medical) on several models. With regard to the safety of these technologies (one death in a cryo-sauna in 2015), the certification of medical devices seems inevitable. The mobility of the devices appears to be important, and this feature will require an optimised means of supplying the devices while they are mobile and a size that is better adapted for installation.

This review contributes to the optimisation of cold treatments offered by health professionals and medical and paramedical personnel (kinesiotherapists, coaches, physical trainers, wellness centre operators, and others). This review will enable professionals to choose the technologies and adapt the protocols best suited to their activities so that they may optimize their services and achieve the desired effects for their patients or customers. Cryotherapy/cryostimulation apparatus producers can also use the scientific results to create more efficient devices that meet market requirements.

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References

Aletaha, D., Neogi, T., Silman, A.J., Funovits, J., Felson, D.T., Bingham, C.O., Birnbaum, N.S., Burmester, G.R., Bykerk, V.P., Cohen, M.D., Combe, B., Costenbader, K.H., Dougados, M., Emery, P., Ferraccioli, G., Hazes, J.M., Hobbs, K., Huizinga, T.W., Kavanaugh, A., Kay, J., Kvien, T.K., Laing, T., Mease, P., Menard, H.A., Moreland, L. W., Naden, R.L., Pincus, T., Smolen, J.S., Stanislawska-Biernat, E., Symmons, D., Tak, P.P., Upchurch, K.S., Vencovsky, J., Wolfe, F., Hawker, G., 2010. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League against Rheumatism collaborative initiative. Arthritis Rheumatol. 62, 2569–2581.

Banfi, C., Melegati, G., Barassi, A., Dogliotti, G., Melzi d'Eril, G., Dugue, B., Corsi, M., 2009. Effects of whole-body cryotherapy on serum mediators of inflammation and serum muscle enzymes in athletes. J. Therm. Biol. 34, 55–59.

Bettoni, L., Bonomi, F.G., Zani, V., Manisco, L., Indelicato, A., Lanteri, P., Banfi, G., Lombardi, G., 2013. Effects of 15 consecutive cryotherapy sessions on the clinical output of fibromyalgic patients. Clin. Rheumatol. 32, 1337–1345.

Bieuzen, F., Louis, J., Hausswirth, C., 2015. Cryothérapie corps entier et exercice. Sci. Sports 30, 113–118.

Bleakley, C.M., Hopkins, J.T., 2010. Is it possible to achieve optimal levels of tissue cooling in cryotherapy? Phys. Ther. Rev. 15, 344–350.

Bleakley, C., Bieuzen, F., Davison Gareth, W., Costello, J., 2014. Whole-body cryotherapy: empirical evidence and theoretical perspectives. Open Access J. Sports Med. 5, 25–36.

Bouzigon, R., Ravier, G., Dugue, B., Grappe, F., 2014. The use of whole-body cryostimulation to improve the quality of sleep in athletes during high level standard competitions. Br. J. Sports Med. 48, 572.

Bugaj, R., 1975. The cooling, analgesic, and rewarming effects of ice massage on localized skin. Phys. Ther. 55, 11–19.

Chatzinikolaou, A., Fatouros, I.G., Gourgoulis, V., Avloniti, A., Jamurtas, A.Z., Nikolaidis, M.G., Douroudos, I., Michailidis, Y., Beneka, A., Malliou, P., Tofas, T., Georgiadis, I., Mandalidis, D., Taxildaris, K., 2010. Time course of changes in performance and inflammatory responses after acute plyometric exercise. J. Strength Cond. Res. 24, 1389–1398.

Cholewka, A., Stanek, A., Sieron, A., Drzazga, Z., 2012. Thermography study of skin response due to whole-body cryotherapy. Skin Res. Technol. 18, 180–187.

Choy, E., 2012. Understanding the dynamics: pathways involved in the pathogenesis of rheumatoid arthritis. Rheumatology 51, 3–11.

Costello, J.T., Algar, L.A., Donnelly, A.E., 2012a. Effects of whole-body cryotherapy (−110 °C) on proprioception and indices of muscle damage. Scand. J. Med. Sci. Sports 22, 190–198.

Costello, J.T., Culligan, K., Selfe, J., Donnelly, A.E., 2012b. Muscle, skin and core

temperature after −110 °C cold air and 8 °C water treatment. PLoS One 7, e48190.
Costello, J.T., Donnelly, A.E., Karki, A., Selfe, J., 2014. Effects of whole body cryotherapy and cold water immersion on knee skin temperature. Int. J. Sports Med. 35, 35–40.
Dugue, B., Leppanen, E., 2000. Adaptation related to cytokines in man: effects of regular swimming in ice-cold water. Clin. Physiol. 20, 114–121.
Dugue, B., Smolander, J., Westerlund, T., Oksa, J., Nieminen, R., Moilanen, E., Mikkelsson, M., 2005. Acute and long-term effects of winter swimming and whole-body cryotherapy on plasma antioxidative capacity in healthy women. Scand. J. Clin. Lab. Investig. 65, 395–402.
Dugue, B.M., 2015. An attempt to improve Ferreira-Junior model concerning the anti-inflammatory action of whole-body cryotherapy after exercise induced muscular damage (EIMD). Front. Physiol. 6, 35.
Ferreira-Junior, J.B., Bottaro, M., Loenneke, J.P., Vieira, A., Vieira, C.A., Bemben, M.G., 2014a. Could whole-body cryotherapy (below −100 °C) improve muscle recovery from muscle damage? Front. Physiol. 5, 247.
Ferreira-Junior, J.B., Bottaro, M., Vieira, A., Siqueira, A.F., Vieira, C.A., Durigan, J.L., Cadore, E.L., Coelho, L.G., Simoes, H.G., Bemben, M.G., 2014b. One session of partial-body cryotherapy (−110 °C) improves muscle damage recovery. Scand. J. Med. Sci. Sports, 524–530.
Fonda, B., Sarabon, N., 2013. Effects of whole-body cryotherapy on recovery after hamstring damaging exercise: a crossover study. Scand. J. Med. Sci. Sports, 270–278.
Fonda, B., De Nardi, M., Sarabon, N., 2014. Effects of whole-body cryotherapy duration on thermal and cardio-vascular response. J. Therm. Biol. 42, 52–55.
Fricke, R., 1989. Ganzkörperkältetherapie in einer kältekammer mit temperaturen um −110 °C. Z. Phys. Med. Balneol. Med. Klimatol. 18, 1–10.
Gizinska, M., Rutkowski, R., Romanowski, W., Lewandowski, J., Straburzynska-Lupa, A., 2015. Effects of whole-body cryotherapy in comparison with other physical modalities used with kinesitherapy in rheumatoid arthritis. BioMed. Res. Int. 2015, 7.
Glickman-Weiss, E.L., Nelson, A.G., Hearon, C.M., Goss, F.L., Robertson, R.J., Cassinelli, D.A., 1993. Effects of body morphology and mass on thermal responses to cold water: revisited. Eur. J. Appl. Physiol. Occup. Physiol. 66, 299–303.
Gordh, T., 1988. Epidural clonidine for treatment of postoperative pain after thoracotomy. A double-blind placebo-controlled study. Acta Anaesthesiol. Scand. 32, 702–709.
Gran, J.T., Skomsvoll, J.F., 1997. The outcome of ankylosing spondylitis: a study of 100 patients. Br. J. Rheumatol. 36, 766–771.
Guillot, X., Tordi, N., Mourot, L., Demougeot, C., Dugue, B., Prati, C., Wendling, D., 2014. Cryotherapy in inflammatory rheumatic diseases: a systematic review. Expert Rev. Clin. Immunol. 10, 281–294.
Hammond, L.E., Cuttell, S., Nunley, P., Meyler, J., 2014. Anthropometric characteristics and sex influence magnitude of skin cooling following exposure to whole body cryotherapy. BioMed. Res. Int. 2014, 7.
Hausswirth, C., Louis, J., Bieuzen, F., Pournot, H., Fournier, J., Filliard, J.R., Brisswalter, J., 2011. Effects of whole-body cryotherapy vs. far-infrared vs. passive modalities on recovery from exercise-induced muscle damage in highly-trained runners. PLoS One 6, e27749.
Hausswirth, C., Schaal, K., Le Meur, Y., Bieuzen, F., Filliard, J.R., Volondat, M., Louis, J., 2013. Parasympathetic activity and blood catecholamine responses following a single partial-body cryostimulation and a whole-body cryostimulation. PLoS One 8, e72658.
Herrera, E., Sandoval, M.C., Camargo, D.M., Salvini, T.F., 2010. Motor and sensory nerve conduction are affected differently by ice pack, ice massage, and cold water immersion. Phys. Ther. 90, 581–591.
Hirvonen, H.E., Mikkelsson, M.K., Kautiainen, H., Pohjolainen, T.H., Leirisalo-Repo, M., 2006. Effectiveness of different cryotherapies on pain and disease activity in active rheumatoid arthritis. A randomised single blinded controlled trial. Clin. Exp. Rheumatol. 24, 295–301.
Huttunen, P., Rintamaki, H., Hirvonen, J., 2001. Effect of regular winter swimming on the activity of the sympathoadrenal system before and after a single cold water immersion. Int. J. Circumpolar Health 60, 400–406.
Huttunen, P., Kokko, L., Ylijukuri, V., 2004. Winter swimming improves general well-being. Int. J. Circumpolar Health 63, 140–144.
Jastrzabek, R., Straburzynska-Lupa, A., Rutkowski, R., Romanowski, W., 2013. Effects of different local cryotherapies on systemic levels of TNF-alpha, IL-6, and clinical parameters in active rheumatoid arthritis. Rheumatol. Int. 33, 2053–2060.
Leppaluoto, J., Westerlund, T., Huttunen, P., Oksa, J., Smolander, J., Dugue, B., Mikkelsson, M., 2008. Effects of long-term whole-body cold exposures on plasma concentrations of ACTH, beta-endorphin, cortisol, catecholamines and cytokines in healthy females. Scand. J. Clin. Lab. Investig. 68, 145–153.
Louis, J., Schaal, K., Bieuzen, F., Le Meur, Y., Filliard, J.R., Volondat, M., Brisswalter, J., Hausswirth, C., 2015. Head exposure to cold during whole-body cryostimulation: influence on thermal response and autonomic modulation. PLoS One 10, e0124776.
Lubkowska, A., Chudecka, M., Klimek, A., Szygula, Z., Fraczek, B., 2008. Acute effect of a single whole body cryostimulation on prooxidant- antioxidant balance in blood of healthy, young men. J. Therm. Biol. 33, 464–467.
Lubkowska, A., Dolegowska, B., Szygula, Z., Klimek, A., 2009. Activity of selected enzymes in erythrocytes and level of plasma antioxidants in response to single whole-body cryostimulation in humans. Scand. J. Clin. Lab. Investig. 69, 387–394.
Lubkowska, A., Szygula, Z., Klimek, A.J., Torii, M., 2010. Do sessions of cryostimulation have influence on white blood cell count, level of IL6 and total oxidative and antioxidative status in healthy men? Eur. J. Appl. Physiol. 109, 67–72.
Lubkowska, A., Szygula, Z., Chlubek, D., Banfi, G., 2011. The effect of prolonged whole-body cryostimulation treatment with different amounts of sessions on chosen pro- and anti-inflammatory cytokines levels in healthy men. Scand. J. Clin. Lab. Investig. 71, 419–425.
Lubkowska, A., Dołęgowska, B., Szyguła, Z., 2012. Whole-Body cryostimulation – potential beneficial treatment for improving antioxidant capacity in healthy men – significance of the number of sessions. PLoS One 7, e46352.
Lubkowska, A., Dołęgowska, B., Szyguła, Z., Bryczkowska, I., Stańczyk-Dunaj, M., Sałata, D., Budkowska, M., 2013. Winter-swimming as a building-up body resistance factor inducing adaptive changes in the oxidant/antioxidant status. Scand. J. Clin. Lab. Investig. 73, 315–325.
Lubkowska, A., Dudzinska, W., Bryczkowska, I., Dolegowska, B., 2015. Body composition, lipid profile, adipokine concentration, and antioxidant capacity changes during interventions to treat overweight with exercise programme and whole-body cryostimulation. Oxid. Med. Cell. Longev., 2015, Article ID 803197, http://dx.doi.org/10.1155/2015/803197.
Metzger, D., Zwingmann, C., Protz, W., Jäckel, W.H., 2000. Die bedeutung der ganzkörperkältetherapie im rahmen der rehabilitation bei patienten mit rheumatischen erkrankungen. Rehabilitation 39, 93–100.
Mila-Kierzenkowska, C., Wozniak, A., Wozniak, B., Drewa, G., Rakowski, A., Jurecka, A., Rajewski, R., 2009. Whole-body cryostimulation in kayaker women: a study of the effect of cryogenic temperatures on oxidative stress after the exercise. J. Sports Med. Phys. Fit. 49, 201–207.
Mila-Kierzenkowska, C., Jurecka, A., Wozniak, A., Szpinda, M., Augustynska, B., Wozniak, B., 2013. The effect of submaximal exercise preceded by single whole-body cryotherapy on the markers of oxidative stress and inflammation in blood of volleyball players. Oxid. Med. Cell. Longev., 10.
Miller, E., Mrowicka, M., Malinowska, K., Mrowicki, J., Saluk-Juszczak, J., Kedziora, J., 2010. Effects of whole-body cryotherapy on a total antioxidative status and activities of antioxidative enzymes in blood of depressive multiple sclerosis patients. World J. Biol. Psychiatry: Off. J. World Fed. Soc. Biol. Psychiatry 12, 223–227.
Miller, E., 2012. Multiple sclerosis. Adv. Exp. Med. Biol. 724, 222–238.
Miller, E., Saluk, J., Morel, A., Wachowicz, B., 2013. Long-term effects of whole body cryostimulation on uric acid concentration in plasma of secondary progressive multiple sclerosis patients. Scand. J. Clin. Lab. Investig. 73, 635–640.
Miller, E., Kotska, J., Wlodarczyk, T., Dugue, B., 2016. Whole body cryostimulation provides benefits for fatigue and functional status in multiple sclerosis patients. Acta Neurol. Scand. . http://dx.doi.org/10.1111/ane.12557
Nestler, E.J., Barrot, M., DiLeone, R.J., Eisch, A.J., Gold, S.J., Monteggia, L.M., 2002. Neurobiology of depression. Neuron 34, 13–25.
Nugraha, B., Gunther, J.T., Rawert, H., Siegert, R., Gutenbrunner, C., 2015. Effects of whole body cryo-chamber therapy on pain in patients with chronic low back pain: a prospective double blind randomised controlled trial. Eur. J. Phys. Rehabil. Med. 51, 143–148.
Ostrowski, K., Rohde, T., Asp, S., Schjerling, P., Pedersen, B.K., 1999. Pro- and anti-inflammatory cytokine balance in strenuous exercise in humans. J. Physiol. 515, 287–291.
Paddon-Jones, D.J., Quigley, B.M., 1997. Effect of cryotherapy on muscle soreness and strength following eccentric exercise. Int. J. Sports Med. 18, 588–593.
Parsons, K.C., 2002. The effects of gender, acclimation state, the opportunity to adjust clothing and physical disability on requirements for thermal comfort. Energy Build. 34, 593–599.
Pertovaara, A., Kauppila, T., Jyväsjärvi, E., Kalso, E., 1991. Involvement of supraspinal and segmental alpha-2-adrenergic mechanism in the medetomidine-induced antinociception. Neuroscience 44, 705–714.
Pertovaara, A., Kalmari, J., 2003. Comparison of the visceral antinociceptive effects of spinally administered MPV-2426 (fadolmidine) and clonidine in the rat. Anesthesiology 92, 189–194.
Pournot, H., Bieuzen, F., Louis, J., Mounier, R., Fillard, J.R., Barbiche, E., Hausswirth, C., 2011. Time-course of changes in inflammatory response after whole-body cryotherapy multi exposures following severe exercise. PLoS One 6, e22748.
Rymaszewska, J., Ramsey, D., 2008. Whole body cryotherapy as a novel adjuvant therapy for depression and anxiety. Arch. Psychiatry Psychother. 2, 49–57.
Rymaszewska, J., Ramsey, D., Chladzinska-Kiejna, S., 2008. Whole-body cryotherapy as adjunct treatment of depressive and anxiety disorders. Arch. Immunol. Ther. Exp. 56, 63–68.
Samuels, C., 2008. Sleep, recovery, and performance: the new frontier in high-performance athletics. Neurol. Clin. 26, 169–180.
Savic, M., Fonda, B., Sarabon, N., 2013. Actual temperature during and thermal response after whole-body cryotherapy in cryo-cabin. J. Therm. Biol. 38, 186–191.
Schaal, K., Le Meur, Y., Bieuzen, F., Petit, O., Hellard, P., Toussaint, J.F., Hausswirth, C., 2013. Effect of recovery mode on postexercise vagal reactivation in elite synchronized swimmers. Appl. Physiol. Nutr. Metab. 38, 126–133.
Schaal, K., Le Meur, Y., Louis, J., Filliard, J.R., Hellard, P., Casazza, G., Hausswirth, C., 2014. Whole-body cryostimulation limits overreaching in elite synchronized swimmers. Med. Sci. Sports Exerc., 1416–1425.
Selfe, J., Alexander, J., Costello, J.T., May, K., Garratt, N., Atkins, S., Dillon, S., Hurst, H., Davison, M., Przybyla, D., Coley, A., Bitcon, M., Littler, G., Richards, J., 2014. The effect of three different (−135 °C) whole body cryotherapy exposure durations on elite rugby league players. PLoS One 9, e86420.
Siems, W., Brenke, R., 1992. Changes in the glutathione system of erythrocytes due to enhanced formation of oxygen free radicals during short-term whole body

cold stimulus. Arct. Med. Res. 51, 3–9.
Smolander, J., Mikkelsson, M., Oksa, J., Westerlund, T., Leppaluoto, J., Huttunen, P., 2004. Thermal sensation and comfort in women exposed repeatedly to whole-body cryotherapy and winter swimming in ice-cold water. Physiol. Behav. 82, 691–695.
Stanek, A., Cholewka, A., Galuda, J., Drzazga, Z., Sieron, A., Sieron-Stoltny, K., 2015. Can whole-body cryotherapy with subsequent kinesiotherapy procedures in closed type cryogenic chamber improve BASDAI, BASFI, and some spine mobility parameters and decrease pain intensity in patients with ankylosing spondylitis? BioMed. Res. Int., Article ID 404259, http://dx.doi.org/10.1155/2015/404259
Stankovic, M., Radovanovic, D., 2012. Oxidative stress and physical activity. SportLogia 8, 1–11.
Sutkowy, P., Augustynska, B., Wozniak, A., Rakowski, A., 2014. Physical exercise combined with whole-body cryotherapy in evaluating the level of lipid peroxidation products and other oxidant stress indicators in kayakers. Oxid. Med. Cell. Longev., 7.
Szczepanska-Gieracha, J., Borsuk, P., Pawik, M., Rymaszewska, J., 2013. Mental state and quality of life after 10 sessions whole-body cryotherapy. Psychol. Health Med. 19, 40–46.
Trinanes, Y., Gonzalez-Villar, A., Gomez-Perretta, C., Carrillo-de-la-Pena, M.T., 2014. Profiles in fibromyalgia: algometry, auditory evoked potentials and clinical characterization of different subtypes. Rheumatol. Int. 34, 1571–1580.
Urso, M.L., Clarkson, P.M., 2003. Oxidative stress, exercise, and antioxidant supplementation. Toxicology 189, 41–54.
Westerlund, T., Oksa, J., Smolander, J., Mikkelsson, M., 2003. Thermal responses during and after whole-body cryotherapy (−110 °C). J. Therm. Biol. 28, 601–608.
Westerlund, T., Uusitalo, A., Smolander, J., Mikkelsson, M., 2006. Heart rate variability in women exposed to very cold air (−110 °C) during whole-body cryotherapy. J. Therm. Biol. 31, 342–346.
Wozniak, A., Mila-Kierzenkowska, C., Szpinda, M., Chwalbinska-Moneta, J., Augustynska, B., Jurecka, A., 2013. Whole-body cryostimulation and oxidative stress in rowers: the preliminary results. Arch. Med. Sci. 9, 303–308.
Yamauchi, T., 1988. Whole-body cryotherapy is a method of extreme cold (−175 °C) treatment initially used for rheumatoid arthritis. Z. Phys. Med. Balneolo. Med. Klimatol. 15, 311.
Zagrobelny, Z., Halawa, B., Negrusz-Kawecka, M., Spring, A., Gregorowicz, H., Wawrowska, A., Rozwadowski, G., 1992. Hormonal and hemodynamic changes caused by whole body cooling in patients with rheumatoid arthritis. Pol. Arch. Med. Wewn. 87, 34–40.
Zalewski, P., Klawe, J.J., Pawlak, J., Tafil-Klawe, M., Newton, J., 2013. Thermal and hemodynamic response to whole-body cryostimulation in healthy subjects. Cryobiology, 295–302.
Ziemann, E., Olek, R.A., Kujach, S., Grzywacz, T., Antosiewicz, J., Garsztka, T., Laskowski, R., 2012. Five-day whole-body cryostimulation, blood inflammatory markers, and performance in high-ranking professional tennis players. J. Athl. Train. 47, 664–672.
Ziemann, E., Olek, R.A., Grzywacz, T., Kaczor, J.J., Antosiewicz, J., Skrobot, W., Kujach, S., Laskowski, R., 2014. Whole-body cryostimulation as an effective way of reducing exercise-induced inflammation and blood cholesterol in young men. Eur. Cytokine Netw. 25, 14–23.