THE EFFECTS OF WHOLE-BODY CRYOTHERAPY

EXPOSURE IN SPORT: APPLICATIONS FOR RECOVERY

AND PERFORMANCE

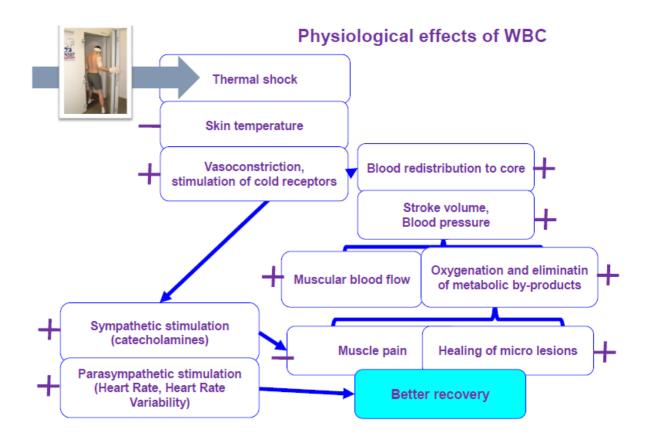
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Introduction

Local cold therapy or cryotherapy is commonly used to relieve pain, particularly pain caused by inflammatory diseases, injuries and overuse symptoms. A specific form of cold therapy or stimulation was proposed 30 years ago to treat rheumatic diseases. This therapy involves brief exposure of the whole body in special temperature-controlled cryochambers, where the air is maintained at -110 °C to -140 °C. The treatment was named whole-body cryotherapy (WBC) and its effects are presented in Figure 1. WBC is generally applied for 2 minutes, but in some protocols it can last for up to 3 minutes. Exposure can involve a single subject, or a small group of subjects - up to four people can be present in the chamber at the same time. Before entering the cryochamber, each subject spends 30 seconds in a vestibule at a temperature of -60 °C to allow temperature adaptation. During exposure, subjects wear minimal clothing; to avoid frostbite they wear shorts (bathing suit), socks, clogs or shoes, surgical mask, gloves, and a hat (or headband) covering the ears. Subjects are dried of any sweat before entering the cryo facility, where the air is clear and dry. This treatment can help to relieve pain and inflammatory symptoms caused by numerous disorders, particularly those associated with rheumatic conditions, and it is recommended for the treatment of arthritis, fibromyalgia and ankylosing spondylitis. Very recently, whole-body exposure to cold was shown to aid post-exercise recovery by altering blood flow [11] and improving perceived recovery. Exposure of the body to cold may also exert significant effects on post-exercise recovery at the cardiovascular level. As exercise causes intensity-dependent parasympathetic withdrawal and a sympathetic increase, prompt recovery of parasympathetic activity is desirable after exercise. The effects of dry air whole-body cryostimulation (classically ranging from -110 °C to -160 °C) on post-exercise autonomic recovery are not well documented, even though this recovery method is increasingly used in the sporting realm.



 $Fig. \ 1. \ Physiological \ effects \ of \ WBC \ exposure \ (\textit{Adapted from} \ Hausswirth \ and \ Mujika, \ 2013)$

The aim of this article was to review what is known about WBC in the context of exercise, particularly in the context of recovery. We note that the scientific knowledge has been extended both in terms of the number of articles (which have doubled) and their quality over the last 5 years, with more than 250 references from a range of scientific fields and research themes available today. The number of whole-body or partial cryotherapy devices available in France is constantly increasing, making this a widely available technique for French athletes. It therefore appears necessary to offer a review of the data which will complement previously published reviews. The aim of this review is to

allow athletes and trainers to undertake actions based on scientific evidence, but also to define the limits, identify the new questions that arise and the research perspectives for this tool.

How exposing the body to cold affects tissue temperatures?

WBC is mainly offered as a tool to rapidly cool various tissues by applying a strong temperature gradient between the inside and the outside of the body. Examination of recent studies makes it possible to objectively review whether this approach is effective. Indeed, despite extreme temperatures of down to -180 °C measured at the outlet in nitrogen-based devices, the decreases in temperature recorded on the skin (-4 °C to -14 °C), in the muscles (≈ -1.1 °C) or for core temperature (\approx -0.3 °C) remain modest. In particular, these differences are lower in magnitude than those measured when ice packs are applied or with protocols involving immersion in cold water [2]. The reason for these differences is relatively simple to understand given the laws of thermodynamics, in particular for the coefficient of thermal conductivity ($k = W/m^2 - K$) which reflects a material's capacity to transfer heat. As air has a lower heat transfer coefficient (0.024 k) than ice (2.18 k) or water (0.58 k), its capacity to extract cold from the body is limited compared to the two other cryotherapy methods. Nevertheless, in the case of WBC, this reduction in heat-extraction is partly compensated for by the fact that a much larger body surface area is exposed than with the other techniques. The extent of this surface appears to play an important role in skin cooling, as recent studies have shown significant differences depending on whether the system is open (e.g. individual compartment) or closed (e.g. cold room). Thus, it appears that in open systems the cooling effect on the body is less significant since the gas rises, whereas in closed systems, cooling is more homogeneous, inducing a greater reduction in mean skin temperature over the whole body. All of these studies indirectly raise the question of the optimal duration of exposure; only one study has attempted to provide an answer so far [3]. According to the authors of this study, exposure to -135 °C for 2 min after 30 s at -60 °C would be adequate for a population of professional rugby players. However, they also indicate that, given the specificity of the population and the markers examined, it is difficult to derive a general protocol from these results. Despite this drawback, this study clearly posed the question and developed a method to attempt to glean a response. Other methods could also be envisaged, for example mathematical modelling of the individual thermal characteristics based on simple data (height, % body fat, gender, etc.) as is already the case for other cold-based therapies. Because of the lack of data, it appears difficult today to set out precise recommendations on the optimal durations, frequencies and/or exposure surfaces without having previously defined thresholds for the desired target temperature. These thresholds depend on the tissues, what took place before the therapy, and the objective of the WBC (i.e., therapeutic, recovery, etc.). In this context, current recommendations mainly advise caution to avoid potential side effects, but further investigations should lead to tailored protocols with improved efficacy.

HOW MANY WBC SESSIONS ARE REQUIRED TO ACCELERATE RECOVERY IN SPORT?

Several studies have tested the efficacy of WBC sessions on functional recovery in a nondisease context. The first of these studies examined exercise-induced muscle damage, later studies were performed in more everyday conditions. Application of WBC during the post-exercise recovery period has now been tested with many sports such as synchronised swimming, tennis, canoeing, and running in rough terrain such as in trail running or rugby [4-8]. The results of these studies indicate weak effects of WBC on recovery when it is used after exercises performed in a laboratory inducing moderate to severe localised muscle damage. In contrast, a significant improvement in functional recovery compared to a passive recovery situation was observed when WBC was used after exercise performed in real-life conditions. It is interesting to note that the beneficial effects of WBC appear from the first exposure after fatiguing exercise and do not seem to be enhanced by repeated exposures. However, until this year, no study had attempted to introduce a placebo condition. In the vast majority of studies, functional recovery was assessed by measuring physical performance, which is likely to be affected by a placebo effect. In a recent German study, published in January 2015, a placebo condition was introduced for the first time [8]. The results of this study indicate that, compared to the placebo condition, WBC is associated with an improvement in early recovery after intermittent high-intensity exercises. It therefore appears that, in this very specific case, WBC presents a significant advantage, confirming the results of other studies applying cold water immersion. In contrast, WBC appears to be only mildly beneficial in functional terms when used during short-term recovery before exercises inducing muscle damage. Persistent use of WBC after exercise inducing mild to moderate muscle damage could actually be counter-productive as it potentially inhibits the anabolic process. Indeed, a recent study of this type of exercise associated with cold water immersion-based methods indicated that chronic exposure to cold limits muscle development and reduces gains in strength production compared to non-cold-based recovery techniques [9].

In summary, it appears today that there is evidence that WBC can facilitate functional recovery after exercise inducing mild muscle damage (i.e., reduced capacity for immediate force production <20%, rapid functional recovery (<48 h) and [CK] $_{plasma/serum}$ < ~1000 UI/L), which is of intermittent type at high intensity and is performed in real-life conditions. In contrast, when more extensive muscle

damage is induced, or WBC is used repeatedly after muscle-building sessions, its capacity to promote functional recovery has not been demonstrated.

EFFECTS OF WBC ON DELAYED ONSET MUSCLE SORENESS (DOMS)

Even though cold is very frequently suggested to limit muscle damage in the scientific literature, few studies using WBC have investigated this aspect. On the whole, the studies that have, showed that the benefits of WBC were low compared to a control condition, whether applied after exercises inducing significant muscle damage (repeated eccentric contractions) or mild muscle damage (repeated tennis training or mountaineering races). These results were recently confirmed in a Cochrane meta-analysis indicating that, after exercise inducing muscle damage or after exercise in real-life conditions, plasma creatine kinase, lactate dehydrogenase or aspartate aminotransferase levels were only mildly affected by one or more WBC sessions compared to a control condition [10]. An increase in serum creatine kinase (CK) is the most typical indicator of exertional rhabdomyolysis, and assay of this marker could be used to determine physical workload, recovery and possible overtraining. The benefits of cold-based recovery have been described in top-level rugby players after training, where immersion of the legs in cold water resulted in a decrease in total serum CK concentrations compared to passive recovery [21]. This confirmed the results of Gill et al., [22] who also measured CK levels in the interstitial fluid surrounding the muscles in rugby players. WBC induced a clear and significant decrease in the mean values of CK and lactate dehydrogenase (LDH) after 1 week of treatment in professional rugby players. It seems that short-lived exposure to cold air enhances muscle fibre repair, limiting the breakdown of the cell membrane or reducing its increased permeability. These effects are generally caused by oxidising agents produced during physical exercise. Since the athletes did not change their training scheme or load during the period of WBC treatment, the significant decrease in total serum CK and LDH concentrations led to effective and rapid recovery from muscle damage.

Understanding the impact of cold on the immune system and

INFLAMMATION

Classical immunological markers such as immunoglobulins (Ig) and C-reactive protein (CRP) were measured in athletes before and after a treatment cycle. These markers are both regularly and easily measured in the general population and in athletes as markers of acute or chronic infection and/or inflammation. In rugby players who underwent WBC treatment, immunoglobulins were slightly, but

not significantly, increased, and CRP showed a slight, but also not significant, decrease. The lymphocyte and monocyte counts were unchanged: 44.7% (standard deviation (SD) 8.2) for lymphocytes before WBC and 37.8% (SD 10.6) after (p-value not significant), and 9.6% for monocytes in both blood samples (SD 1.7 before, 3.5 after; p-value not significant) [23]. Thus, WBC is not associated with alterations to immunological markers, and it does not appear to have a detrimental effect on the immune system. Other data suggest that WBC does not impact immunological parameters, although the period of observation in this study was too short to assess modifications to lymphocyte involvement and function. In fact, subjecting healthy males to prolonged cold water immersion resulted in slight increases in plasma tumour necrosis factor-a levels, and lymphocyte and monocyte counts.

There is thus limited evidence that short- or long-lived exposure to cold causes immunosuppression. Rather, cold exposure has an immunostimulating effect possibly related to the enhanced noradrenaline (norepinephrine) response triggered by cold. Therefore, a stimulating effect of cold exposure could be argued. This effect is regulated by the relationship between the decrease in core temperature and the duration of exposure.

Although exposure to cold is very extensively used to limit inflammation triggered by physical exercise, or in the context of inflammatory diseases, its physiological effects on the processes involved remain poorly known. A few studies showed a significant effet of WBC on the inflammatory process after exercises inducing mild muscle damage. Thus, an increase in IL-1ra associated with a reduction in IL-1 β and in CRP was observed after a WBC session following simulated trail running lasting less than 2 h [11] [see Fig. 2A, B and C]. Similarly, a reduction in IL-6, and IL-1 β levels was observed when a WBC session was scheduled before 40 min exercise [12]. These recent results reinforce observations by Banfi *et al.* [13] (although their study did not include a control group) indicating that 5 WBC sessions in athletes reduced the level of soluble intracellular adhesion molecules (sICAM-1), the pro-inflammatory response, as attested by PGE2, IL-2, IL-8 levels, and increased levels of the anti-inflammatory cytokine IL-10.

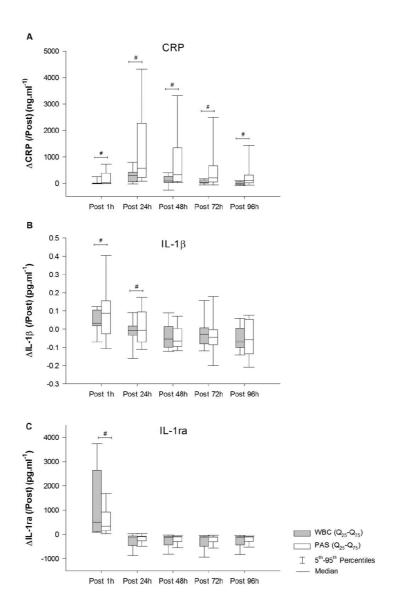


Fig. 2. Changes in CRP (A), IL-1b (B) and IL-1ra levels (C) between immediately post-running exercise and during recovery. #, significant difference between groups (p,0.05). WBC, whole-body cryotherapy; PAS, passive rest recovery (*Adapted from* Pournot et al. 2011).

Based on all these observations, the beneficial effects of WBC on recovery from muscle damage and/or functional recovery could be explained by a reduction in the inflammatory process. A Brazilian team has hypothesised that WBC could modify the thermoregulatory response [14], causing an acceleration in recovery from exercise-induced muscle damage by reducing circulating sICAM-1 levels. This would lead to reduced migration of neutrophils and lymphocytes to the muscle tissue, thus inducing a diminished pro-inflammatory response, and release of free radicals, as well as an increase in the anti-inflammatory response.

HOW WBC AFFECTS ANTIOXIDANT STATUS?

Several studies have measured the effets of single or repeated WBC sessions on oxidative stress and antioxidant function. However, the results were heterogeneous and suffered from several methodological biases, making it difficult to exploit them. Thus, in a study comparing two untrained groups, one of which was regularly exposed to intense cold by WBC, the other not, an increase in the antioxidant status of the first group was observed (see Fig. 3). In contrast, a very minor difference in lipid peroxidation was noted between the groups [15]. Another crossed randomised study of trained canoeists reported a reduction in oxidative stress after 10 days' training in the WBC condition compared to the control condition [16]. However, the enzymatic profiles for the athletes involved in this study were quite unusual and a high degree of inter-individual variation was noted. This result raises significant questions about the relevance of the conclusions that can be drawn from this study. Nevertheless, most studies show an increase in the body's antioxidant capacity when it is regularly exposed to very intense cold. In the context of exercise, some authors suggest that the use of WBC as a recovery method could help promote a balance between pro- and antioxidant reactions, in particular during periods when the training workload is being increased. Nevertheless, several questions remain, among which whether maintaining this equilibrium is an advantage if the objective sought is to promote adaptations to training. In this case, an imbalance could, to a certain extent, act as a stimulant.

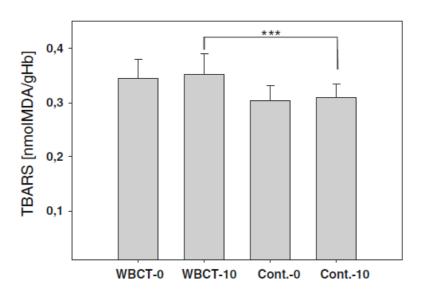


Fig. 3. The effect of whole-body cryostimulation (WBCT) on the level of thiobarbituric acid reactive substances (TBARS) in plasma. WBCT study group before (WBCT-0) and after 10 days of cryostimulation (WBCT-10); non-WBCT control subjects at the start of the experiment (Cont.-0) and 10 days later (Cont.-10); Error bars indicate standard deviation (SD). (*P < 0.05, **P < 0.01, ***P < 0.001) Adapted from Miller et al. 2012.

THE AUTONOMIC NERVOUS SYSTEM IS INFLUENCED BY WBC EXPOSURE

Few studies have addressed the question of how WBC affects the nervous system. However, these few studies all indicated that WBC modified the activity of the autonomous nervous system. A French team, in particular, showed that a 3-min exposure to very intense cold increased the activity of the autonomous nervous system with a predominance of the parasympathetic branch [17]. In this study, the increase in sympathetic activity was measured through an increase in plasma catecholamine concentrations, while a reduction in heart rate associated with an increase in indicators of cardiac variability indicated an increase in parasympathetic activity. According to the authors, the effect on parasympathetic activity is greater with WBC than with partial cryotherapy, suggesting that a signficant reduction in skin temperature is necessary to maximally stimulate the autonomous nervous system. Similar results were reported in training conditions, with an increase in parasympathetic reactivation after exhausting exercise followed by a WBC session [5]. The control group in this study used a passive recovery method. Although not extensively studied, the influence of WBC on the activity of the autonomous nervous system, and in particular on parasympathetic activity, is essential as parasympathetic activity is directly implicated in post-exercise recovery and strongly correlated with sleep quality and life expectancy. New questions thus arise, in particular how long the effects of WBC on the autonomous nervous system last. Are these effects transitory? Are they influenced by the number of daily exposures? Are they affected by temperature?

Numerous studies have accumulated scientific evidence supporting the beneficial effects of WBC in the medical domain - when used as an alternative treatment or rehabilitation technique - and in the sporting realm - especially in the context of post-exercise recovery. However the physiological mechanisms responsible for the effects of extreme cold exposure remain unclear and no consensus on a scientifically-determined optimal cryotherapy protocol has yet been reached. In recently published work from our team, we showed that stimulation of the autonomic nervous system after a single whole-body cryostimulation session was more pronounced when subjects used a cryotherapy system (exposing the whole body to air at -110 °C -140'C air) compared to an open tank (exposing the whole body except the head to expanded nitrogen gas at -160 °C) [17]. The cryochamber system was found to induce the greatest overall decrease in skin temperature, thus raising the question of whether the physiological adaptations to cryotherapy were induced by cold intensity or exposure of the head to cold. We went on to study the specific/isolated influence of exposing the head to cold during five daily cryostimulation sessions causing a similar decrease in skin temperature [19]. Exposure of the body to cold is an effective method to easily and rapidly increase parasympathetic activity, and greater effects are obtained using air-based cryotherapy protocols than with cold water

immersion. Two main modalities of air-based cryotherapy exist: in one, the head is exposed, while in the other it is not. (The head can be submerged in a Cryopod as the subject is exposed to cooled air rather than Ln2 vapour) Thus, our results give indications as to the usefulness of these different techniques and information on the physiological mechanisms involved. Our results indicated that both cryotherapy techniques triggered a relatively similar parasympathetic stimulation without marked effects on recorded variables due specifically to head cooling. These results suggest that the intensity of the autonomic response (i.e., parasympathetic stimulation) is mainly proportional to the intensity of cold experienced, rather than whether the head is cooled or not. It is also possible that the short-lived exposure to cold (3 min) in cryotherapy may not be sufficient to trigger parasympathetic stimulation through the trigeminal nerve endings, as trigeminal afferents are mostly unmyelinated fibres, suggesting that there is a certain latency in their response [20]. A predominance of parasympathetic tone was recorded from the first to the fifth WBC and PBC (Partial Body Cryotherapy) sessions, with small differences between groups in the magnitude of the response.

COULD WBC IMPROVE ATHLETE'S SLEEP QUALITY?

The question of sleep is central to both sporting and cognitive performance today. More specifically, many scientists, doctors, physiotherapists, trainers and athletes consider sleep to be one of the three pillars of recovery, along with nutrition and hydration. Despite this observation, sleep and its quality remain little investigated. The first studies to test the effects of WBC on sleep involved patients with rheumatoid diseases, particularly patients with fibromyalgia. These studies suggested that WBC and other more classical therapies could limit the sleep disturbance experienced by these patients. In the sporting context, two very recent studies indicated that WBC could improve sleep quality, particularly during phases when the training workload is increased [6, 18]. During intense training periods, a deterioration in sleep is commonly reported (with sleep latency, reduced duration and efficacy of sleep); these effects were not observed when athletes were exposed to very intense cold on a daily basis. Exposure to cold could thus help athletes to better support the training workload, consequently limiting the symptoms associated with overreaching such as reduced sleep, increased fatigue or diminished physical capacities.

In a recent study [6], we showed that the periods of intense training performed over the months preceding the major swimming competitions led to the appearance of early symptoms of functional overreaching, including impaired autonomic and metabolic responses to exercise, increased perceived fatigue and deteriorated sleep quantity and quality (see Table 1). This study used a longitudinal design to investigate the effectiveness of WBC as a daily recovery strategy during

intensified training. The results suggested that several of the physiological indicators of fatigue accumulation observed in the

control condition could be reduced by daily WBC sessions. Thus, WBC improved the quality of recovery for swimmers by preserving sleep quantity, preventing an increase in perceived fatigue, and by mitigating the decrease in performance and associated physiological changes during exercise, all of which were observed in the control population.

	BASE	$\mathbf{IT}_{\mathbf{WBC}}$	IT_{CON}	SWC		BASE vs IT _{WBC}	BASE $vsIT_{CON}$	IT_{WBC} vs IT_{CON}
Bed Time					Difference ^A	40. 2 (19.8; 60.6)	49.3 (31.8; 66.8)	-9.1 (-27.3; 9.0)
(h:min)	22:52 ± 0:10	23:32 ± 0:09	23:41 ± 0:10	4.5	% Chance. ^B	99/0/0	100/0/0	66/25/9
		**	**		Clin. Inf. ^C	V.L. harmful	M.L. harmful	Unclear
Get up					Difference A	52.1 (36.4; 67.8)	38.9 (26.4; 51.4)	13.2 (-4.0;30.4)
Time	7:24 ± 0:07	$8:16 \pm 0:07$	$8:03 \pm 0:07$	3.6	% Chance. ^B	100/0/0	100/0/0	5/13/82
(h:min)		***	***		Clin. Inf. ^C	M.L. harmful	M.L. harmful	L. beneficial
Time spent					% Difference ^A	2.5 (-3.1; 8.4)	-2.3 (-5.9; 1.3)	4.9 (1.7;8.2)
in bed	8:32 ± 0:13	$8:43 \pm 0:05$	$8:19 \pm 0:08$	1.4%	% Chance. ^B	64/23/13	5/26/69	97/3/0
(h:min)					Clin. Inf. ^C	Unclear	Unclear	V.L beneficial
Actual Sleep					%Difference ^A	0.6 (-4.3; 5.7)	-4.7 (-7.5; -1.8)	5.5 (2.3;8.8)
duration	$7:13 \pm 0:11$	$7:15 \pm 0:07$	6:53 ± 0:09	1.3%	% Chance B	39/36/25	0/3/97	98/2/0
(h:min)			*#		Clin. Inf. ^C	Unclear	V.L. harmful	V.L beneficial
Sleep					%Difference ^A	25.4 (-20.1; 96.8)	45.0 (6.7;97.0)	-13.5 (-36;16.9)
Latency	17± 2	23 ± 4	28 ± 6	9.3%	% Chance ^B	72/16/12	95/4/1	10/24/'66
(min)			*		Clin. Inf. ^C	Unclear	M.L. harmful	Unclear
Sleep					%Difference ^A	-1.9 (-3.4; -0.4)	-2.3 (-4.1; -0.6)	0.5 (-1.4;2.4)
Efficiency	84.7 ± 1.3	83.1 ± 1.1	82.7 ± 1.6	0.3%	% Chance B	2/2/96	1/2/97	59/16/25
(%)			*		Clin. Inf. ^C	V.L. harmful	V.L. harmful	Unclear
% Time					%Difference ^A	12.0 (6.5; 17.9)	8.7 (2.9; 14.9)	3.0 (-2.0; 8.3)
spent	14.1 ± 0.8	15.9 ± 1.0	15.5 ± 1.1	3.1%	% Chance ^B	99/1/0	94/6/0	49/48/3
moving		*	*		Clin. Inf. ^C	V.L. harmful	L. harmful	P. beneficial
Perceived					%Difference ^A	2.8 (-2.4;8.30)	9.9 (0.2; 20.5)	-6.5 (-1.6; 16.2)
Fatigue	4.2 ± 0.4	4.3 ± 0.4	4.5 ± 0.4	3.0%	% Chance B	47/49/4	88/10/2	3/19/'78
(1-7)			*		Clin. Inf. ^C	P. harmful	L. harmful	L. beneficial
								-0.8 (-12.1;
Perceived					%Difference ^A	3.1 (-5.3; 12.2)	2.2 (-9.8; 15.8)	11.9)
Sleep	4.5 ± 0.3	4.5 ± 0.4	4.5 ± 0.4	3.0%	% Chance ^B	10/89/1	16/78/6	8/81/11
Quality (1-7)					Clin. Inf. ^C	Unlikely	Unclear	Unclear

Table 1. Sleep actigraphy and sleep questionnaire variables. Each questionnaire item was rated on a scale from 1 to 7 (from best to worst in ascending order). Different from BASE: * p < 0.05, *** p < 0.001. Different from ITWBC: # p < 0.05. SWC, smallest worthwhile change, calculated at 0.3*CV from 2-week follow up during normal training. A, Difference in mean. B, % chance that the true value is mechanistically or clinically substantially positive, trivial, or negative. C, clinical inference. V.L., very likely; M.L., most likely; L., likely; P., possibly. (*Adapted from* Schaal et al. 2015)

CONCLUSION AND TAKE-HOME MESSAGES

Today, we better understand the utility of WBC in the specific context of exercise, whether related to the mechanisms it triggers or the way in which it is applied. A change has occurred in the themes addressed in scientific publications in recent years. Thus, the earlier studies investigated the effects of WBC on functional recovery from exercise-induced muscle damage. Today, other paths are explored such as how WBC affects symptoms of depression or sleep quality in situations where the training workload increases. The results are extremely promising, even if they will need to be consolidated.

Research is well underway, in order to gain a better understanding of the physiological mechanisms involved in exposure to WBC. Although placebo conditions are difficult to implement, they are necessary, as are studies of chronic exposure, to better reflect the reality of athletic training. Finally based on scales to assess bias in studies, the levels of effectiveness of WBC require further study. To increase the strength of results, it will be necessary in future studies to limit quality-related biases through better randomisation, systematic anonymisation of subjects, data and conditions, and appropriate statistical handling of data. The clinical results to date, suggest WBC could well become an essential recovery tool, in the ever increasing demands of modern sport.

Based on current knowledge and taking into account the limits mentioned above, we propose the following summary table:

Effects	Training situations		Functional recovery	Muscle damage	Immune and inflammatory response	Antioxidant status	Autonomous nervous system	Sleep	Adaptations to training
Acute	Inducing	Light	©	☺	©©	©			
	muscle damage	Moderate or strong	⊕	:	(()				
	Absence of muscle damage (real-life conditions)		© ©			©	©©		
Chronic	Muscle-buildin								? 😊
	Intermittent training	high-intensity							? ☺
	Increase of the training workload							©©	

[©]Significant positive effects; ©Weak positive effects; ©No positive effect or lack of consensus; ©Potentially negative effect (?©) or positive effect (?©) but we currently lack specific scientific proof for WBC.

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