JOURNAL CLUB

Is the ice bath finally melting? CWI is no greater than active recovery upon local and systemic inflammatory cellular stress in humans.

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Over the past decade, significant research has focussed on optimising the recovery of elite athletes. The premise behind such a theory is that sub-optimal recovery often leads to fatigue, reducing the quality of subsequent training sessions and/or competitive performances, whilst potentially hindering adaptive processes. There is now a plethora of research focussing on the impact of one such recovery strategy, cold-water immersion (CWI), and the benefits it may provide post-exercise.

Proposed mechanisms of action are hypothesised to be a combined result of reduced perception of pain via decreased nerve conduction velocity alongside temperature and pressure induced changes in blood flow and reduced skeletal muscle temperature. As such, cold temperatures may facilitate enhanced recovery from exercise by reducing intramuscular temperature and metabolism, thereby limiting hypoxic stress and the generation of reactive oxygen species (ROS). A cold-induced reduction in muscle blood flow has been traditionally proposed to limit inflammatory signalling, oedema and thus any subsequent secondary damage to the muscle fibres (Mawhinney et al. 2013). It is perhaps important to note that inflammation, oedema and swelling are not synonymous terms. For example, CWI may provide benefits to recovery in the acute period following intense or muscle damaging exercise by limiting oedema and swelling *per se*, independent of changes in inflammation. However, more recently the role of CWI strategies to reduce the inflammatory response has been challenged. Although the inflammatory response and

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subsequent oxidative stress may contribute to so called 'secondary damage', they have been demonstrated to be important to the cell signalling and remodelling processes involved in the post-exercise adaptive response of skeletal muscle (Peake et al. 2015). Indeed, this is highlighted by cytokines and chemokines recruiting inflammatory cells, such as neutrophils and macrophages, to assist with repair. Despite this, the impact of CWI upon the inflammatory response within human skeletal muscle has been largely ignored. Many studies focus on performance and subjective measures alongside systemic inflammatory markers in the blood, but without analysis of muscle as a local secretory tissue that produces inflammatory cytokines; more recently dubbed as myokines. Evidence exists from animal studies to suggest a benefit of cryotherapy techniques upon reducing inflammation in muscle injury, however there remains a lack of data available from relevant human experimentation.

In a recent well-designed study in *The Journal of Physiology*, Peake and colleagues (2016) incorporated a number of local (gene expression of a muscle homogenate) and systemic (blood plasma/serum concentration) inflammatory markers to investigate the effectiveness of CWI compared with an active recovery treatment, and investigated the ensuing inflammatory and cellular stress response after a bout of resistance exercise. For this purpose, nine active young men completed single-leg resistance exercise consisting of 45° leg press (6 sets of 8–12 repetitions), single-leg squats (3 sets of 12 repetitions), knee extensions (6 sets of 8–12 repetitions), and walking lunges (3 sets of 12 repetitions), on alternate legs. The participants completed two trials of the same resistance exercise regime. The two trials were separated by 1 week and followed by either an active recovery period (10 min low-intensity self-selected cycling) or CWI (10 min at 10°C). Blood samples were collected pre-exercise, immediately post-exercise, immediately post-recovery and at 30 min, 1, 2, 24 and 48 h after exercise. Muscle biopsies were collected from the vastus lateralis pre-exercise and at 2, 24 and 48 h after exercise. The exercise protocol successfully initiated inflammation and a cellular stress response with greater numbers of neutrophils ($CD66b^+$), macrophages (count: $CD68^+$, and gene expression of CD163), and gene expression of macrophage cell surface receptors (MAC1) across the 48h post-exercise period vs. pre-exercise. Moreover, cytokine and chemokine mRNA expression (IL1β, TNF, IL6, CCL2, CCL4, CCL5, CXCL2, IL8, LIF), neutrophin gene expression (GDNF, NGF), heat-shock protein mRNA expression (HSP70) and systemic creatine kinase activity and cytokines (plasma IL-6 concentration) were all upregulated at different time points following exercise. Furthermore, heat-shock proteins (HSP70, αB-crystallin) were shown to translocate out of the cytosol to cytoskeletal structures post-exercise, suggested by the authors as being vital to the stabilisation and protection of stressed myofibrillar proteins. Importantly, and perhaps

surprisingly based on the traditional notion that CWI reduces inflammation, Peake and colleagues demonstrated that CWI had no impact on inflammatory measures and cellular stress in comparison to the active recovery trial.

As previously discussed, much of the surrounding literature to date has assessed systemic inflammatory markers in the blood. One such study, by White et al. (2014), assessed 4 various CWI protocols (10 and 30 min at 10 °C and 20 °C) versus passive rest after high-intensity sprint exercise (12 maximal sprints of 120 metres, performed every 3 min). Results showed that 10 min of CWI did not significantly reduce plasma concentration of inflammatory markers (IL-6, IL-8, myeloperoxidase) in any of the protocols; on the contrary, CWI in both cold (10 °C) and cool (20 °C) temperatures for 30 min exacerbated the response of IL-8 and myeloperoxidase in the blood following exercise. In addition, work investigating inflammatory markers in the blood often shows little or no effect of CWI, normally in comparison with a passive control. These results, and the results from Peake and colleagues (2016), challenge the mainstream concept of recovery that has been commonplace for decades. For generations, it has been assumed that the application of a cold stimulus reduces the post-exercise inflammatory cellular stress response, without sufficient data to support this theory. Peake et al. (2016) are the first to show no difference in the post resistance-exercise inflammatory and cellular stress response in comparison to an active recovery in human skeletal muscle.

With no reported difference between CWI and active recovery after a series of lower limb resistance exercises (Peake et al. 2016), future research should look to competitions that elicit greater tissue damage and evoke a superior inflammatory response; such as heavy eccentric exercise or unaccustomed events. The difference between positive reductions of inflammation in animal studies and the neutral results shown by Peake et al. (2016) may be a factor of the extent of damage and inflammation caused to the muscle, as suggested by the authors. Further work is required to assess the relationship between post-exercise CWI and inflammatory cellular stress. Moreover, chronic CWI has been implicated in blunting activation of key proteins and satellite cells in skeletal muscle for up to 2 days after strength exercise (Roberts et al. 2015), with a reduction of inflammatory signalling suggested to be responsible. Despite this, Peake and colleagues (2016) highlight the fact that no change in inflammatory markers within human skeletal muscle and blood seen in their study, suggests a cold-induced reduction in the inflammatory response is unlikely a causing factor of the dampened adaptive response to resistance training (Roberts et al. 2015), as both studies originate from the same data. Thus,

further research is required to investigate the mechanisms implicating a chronic-CWI induced dampened response to resistance training, irrespective of inflammatory and cellular stress levels.

Whilst post-exercise CWI research is an ever-evolving area, conflicts of opinion are commonplace. Current research offers the paradox that post-exercise CWI may benefit genes associated with mitochondrial biogenesis and angiogenesis after high intensity exercise (Joo et al. 2016) whilst also having the ability to dampen the response to resistance exercise training (Roberts et al. 2015). There is a need to understand surrounding literature as, whilst it seems there may be no positive (or negative) implications of post-exercise CWI upon the inflammatory and cellular stress response, CWI may be useful for athletes in other ways. To this end, CWI may be useful if not for the benefits of greater functional recovery and improved subsequent performance, then for the reduction in delayed onset muscle soreness and the reported analgesic and placebo properties.

The lack of impact on the post-exercise inflammatory and cellular stress response needs careful attention when translated into practice. Meta-analyses and performance studies conducted in the area show us CWI may be useful within competition settings, particularly those requiring a short turn-around (such as tournament situations, athletic meets and cycling tours), of a particularly damaging nature, or in high environmental temperatures. However, there remains a lack of justification to use CWI regularly during a "pre-season" or preparation phase, particularly where the goal includes a hypertrophic response, due to the potential of dampening the adaptive response to training (Roberts et al. 2015). Currently, further investigation is needed into the correct periodization of CWI whilst recovery programmes require a more individualised approach: with a particular focus on the goals of the athlete, their training/competition schedule and the environment they are in.

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