Turning up the heat: an evaluation of the evidence for heating to promote exercise recovery, muscle rehabilitation and adaptation.

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Running Heading: Muscle heating, recovery and adaptation

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ABSTRACT

Historically, heat has been used in various clinical and sports rehabilitation settings to treat soft tissue injuries. More recently, interest has emerged in using heat to pre-condition muscle against injury. The aim of this narrative review is to collate information on different types of heat therapy, explain the physiological rationale for heat therapy, and to summarise and evaluate the effects of heat therapy before, during and after muscle injury, immobilisation and strength training. Studies on skeletal muscle cells demonstrate that heat attenuates cellular damage and protein degradation (following in vitro challenges/insults to the cells). Heat also increases the expression of heat shock proteins (HSPs), and upregulates the expression of genes involved in muscle growth and differentiation. In rats, applying heat before and after muscle injury or immobilization typically reduces cellular damage and muscle atrophy, and promotes more rapid muscle growth/regeneration. In humans, some research has demonstrated benefits of microwave diathermy (and to a lesser extent, hot water immersion) before exercise for restricting muscle soreness and restoring muscle function after exercise. By contrast, the benefits of applying heat to muscle after exercise are more variable. Animal studies reveal that applying heat during limb immobilization attenuates muscle atrophy and oxidative stress. Heating muscle may also enhance the benefits of strength training for improving muscle mass in humans. Further research is needed to identify the most effective forms of heat therapy and to investigate benefits of heat therapy for restricting muscle wasting in the elderly and those individuals recovering from serious injury or illness.

Key points

- Animal and human trials have shown that various forms of heating can be used in conjunction with exercise or stress to enhance recovery, adaptation and limit muscle atrophy.
- Heating muscle activates protective mechanisms, reduces oxidative stress and inflammation, and stimulates genes and proteins involved in muscle hypertrophy.
- Further studies highlighting differences between various heating modalities will help inform athletes and coaches on the best heating practices for specific situations.

1. INTRODUCTION

Strategies to maximise recovery after exercise training or competition are used to promote adaptation to training loads, reduce the chance of injury, and improve the body's ability to repeat high level performance [1]. Although a recovery strategy is commonly considered as a post-exercise activity, rehabilitation is also an important task to enhance recovery from injury. Rehabilitation has its own activities (such as completing exercises and treatment by a physiotherapist) that help the individual return to normal function as soon as possible.

Heat has historically been used to treat a range of health conditions, including musculoskeletal injuries. Evidence has emerged that heating induces pre-conditioning effects that may protect tissues from subsequent damage. The traditional rationale for using heat has been to stimulate local blood supply and metabolism in tissues. However, it is now recognised that heat also activates more specific molecular events, including changes in gene expression, anti-inflammatory and antioxidant effects, mitochondrial biogenesis, heat shock protein (HSP) expression, and muscle hypertrophy. Heating has been administered to soft tissues in various forms before, during and after exercise and/or muscle injury. In the following narrative review, we describe in more detail the contexts in which heating has been used, together with the functional, physiological and molecular effects of heating. We also evaluate some of the inconsistencies in the literature, and identify new areas for future research. Studies included in this review were found using search terms including 'exercise', 'muscle damage', 'heat stress', 'hot water immersion', 'recovery', and 'heat therapy', or combinations of these search terms. Additional studies were found within reference lists of journal articles.

2. FORMS OF HEATING

To date, heat research has used various methods to heat the whole body or specific body areas. These methods have varied in terms of the equipment used, the timing (e.g., before, during or after exercise and injury), and the 'intensity' (e.g., differences in water temperature, microwave diathermy power).

2.1 Types of Studies

Heat has been applied to muscle cells undergoing differentiation, mechanical stretch and treatment with glucocorticoid drugs [2, 3]. Animal studies have investigated the effects of heat in response to exercise [4], muscle injury [5]or immobilisation/limb unweighting [6]. Other animal studies have employed heating following synergist ablation/compensated hypertrophy [7], whereby one muscle in a group of muscles is removed so that the remaining muscles are forced to work harder and hypertrophy. Human trials have commonly examined the effects of heat before or after eccentric exercise [8], exercise tasks on single or multiple days [9], and (to a lesser extent) during long-term training [10]. Within these studies, outcomes have included measurements of: muscle temperature; muscle strength, swelling and soreness; markers of muscle damage and inflammation, and molecular mechanisms within muscle itself (e.g., HSP expression, oxidative stress, muscle atrophy, and the activity of kinases in the mammalian target of rapamycin (mTOR) pathway).

2.2 Equipment

A variety of equipment has been used for heating muscle/whole body, including microwave diathermy [11], environmental chambers [12], heat and steam generating sheets [10], heat pads

[7], thermal blankets [6], and warm/hot water immersion [8] (Figure 1). The nomenclature of 'warm' and 'hot' water immersion varies in the literature. For example, Skurvydas et al. [13] described 44°C as 'warm' water, whereas Vaile et al. [8] defined 38°C as 'hot' water. For the purposes of this review, we refer to water temperature ≥38.0°C as hot water immersion (HWI) [14], and temperatures from 36.0–38.0°C as 'warm'.

The reported benefits of heat treatment are not limited to one form of these modes of therapy. Muscle temperature is a key factor that mediates the effects of heating, because it influences the expression of HSPs in muscle [11, 13, 15]. Muscle temperature increases by ~7°C after microwave diathermy (150 W, 20 mins) [11], by ~3°C after HWI (44°C for 45 min, waist deep) [13], and by ~1.8°C after ultrasound treatment (1 MHz frequency, 10 min, 1.5 cm^2 intensity) [15]. No studies have compared different heat treatments on the same participants using the same outcomes measures. At present, it is therefore difficult to compare the effects of the various forms of heating. Some forms of heating may be more practical than others. For example, when teams are travelling, it may not always be possible to transport heating equipment, whereas hot water baths may be more accessible. Some of the benefits derived from heating may also be specific to the heating modality used. Future research is recommended comparing different heating modalities on performance and recovery outcomes (i.e., next day performance, soreness, and range of motion).

2.3 Timing

Although the most common time to adopt recovery strategies is post-exercise/post-competition, heat research has also evaluated the effects of applying heat before (pre-heating), or after (post-heating) activity or injury. A small number of studies have also investigated the effects of applying heat during physical activity/exercise or limb immobilisation. The

following sections outline the effects of applying heat before, during or after exercise and different forms of muscular stress.

2.3.1 Pre-Heating

Research on pre-heating has demonstrated improvements [11, 12, 16, 17], no change [18, 19] and potential negative outcomes [7] in exercise performance and muscle recovery models. Details of these studies are summarised in Table 1.

2.3.1.1 Animal Studies.

Animal studies investigating the effects of pre-heating have yielded mixed results. In rats, Garramone et al. [20] used pre-heating (HWI, water temperature not stated, core temperatures maintained at 42.5°C for 20 min, 12 h before ischemia) to restrict lower limb damage resulting from ischemia. Following 90 min of ischemia, the amount of creatine phosphate in skeletal muscle was significantly greater in pre-heated rats compared with non-heated rats. Mitochondrial swelling was similar, whereas disruption of mitochondrial cristae was lower, and fewer autophagic vacuoles were present in muscle from the pre-heated rats compared with the non-heated rats. Collectively, these findings demonstrated that pre-heating helped to attenuate some signs of ischemic injury in skeletal muscle.

Touchberry et al. [17] immersed rats in hot water (41°C, 20 min) 48 h before downhill running to induce muscle injury. Plasma creatine kinase (CK) activity 2 h post-exercise and mononuclear cell numbers in muscle at 48 h post-exercise were lower in the pre-heated rats compared with non-heated rats. Conversely, total muscle protein content and the expression of myosin heavy chain (MHC) neo (a marker of muscle regeneration) were higher in the heat-treated group after post-exercise.

Naito et al. [21] pre-heated rats by placing them in a heated environmental chamber (41°C, 60 min) 6 h before 8 d of hind limb suspension (to induce muscle atrophy). Pre-heated rats demonstrated less muscle loss, and higher soluble protein content compared with non-heated rats.

Kojima et al. [22] used a similar protocol to Naito et al. [21] and placed rats in a heated environmental chamber (41°C, 60 min) 24 h before the rats were injected with a cardiotoxin (to induce muscle necrosis and regeneration) or saline (control group). At 3 d post-injury, there were more Pax7+ satellite cells in muscle from pre-heated rats (both injured and uninjured) compared with the non-heated-uninjured rats. At 28 d post-injury, muscle protein content in pre-heated-injured rats was significantly higher than in non-heated-injured rats.

In contrast with these findings on the benefits of pre-heating before muscle injury or unloading, Frier and Locke [7] demonstrated different effects of pre-heating prior to synergist ablation. In this study, a heat pad was applied to rats to maintain their core temperature at 42°C for 15 min before removing the gastrocnemius muscle in one leg 24 h later to induce hypertrophy in other muscles. Compared with non-heat-treated rats, heat-treated rats showed a smaller increase in total protein in the plantaris muscle, and reduced expression of type I MHC protein at 3, 5 and 7 d after the gastrocnemius muscle was removed. The disparity between the findings of this study [7] and those from the other pre-heating studies described above may arise from differences in the effects of pre-heating before synergist ablation versus muscle injury and unloading. Pre-heating before synergist ablation may pre-condition muscle, thereby attenuating subsequent muscle hypertrophy. By contrast, pre-heating before muscle injury and unloading appears to activate cellular activity and molecular processes that help to restrict atrophy and facilitate regeneration of skeletal muscle.

176 *2.3.1.2 Human Studies.*

177 Human heat trials have reported some beneficial effects of pre-heating (Figure 2; Table 1),
178 but some inconsistencies in the findings also exist. Iguchi and Shields [12] found that compared
179 with sitting in 23°C, sitting in the heat (73°C) within a sauna for 30 min increased muscle
180 relaxation rate following maximal voluntary contractions to fatigue in physically active people.
181 Khamwong et al. found beneficial effects when participants applied hot packs [23] or entered
182 a sauna [24] before eccentric exercise. Specifically, both hot packs and sauna reduced the loss
183 in range of motion of the wrist resulting from eccentric exercise. Hot packs also reduced the
184 deficit in pain threshold, whereas sauna reduced the deficit in grip strength loss, compared with
185 the control group. Skurvydas et al. [13] had subjects complete HWI (44°C, 45 min) before three
186 sets of drop jumps. They observed an increase in jump height and a smaller decrease in jump
187 height 48 h post-exercise compared with when participants were not immersed in hot water.
188 HWI also resulted in a smaller deficit in maximal voluntary contraction (MVC) force for knee
189 extension (knee kept at 90°), lower plasma CK activity, and lower ratings of muscle soreness
190 at 24 and 48 h post-exercise [13].

191 Another commonly used heating modality in human studies is microwave diathermy. This
192 technique involves applying heat to a region of the body, eliciting an increase in deep tissue
193 temperature through microwaves at user-selected intensities, without heating the skin to
194 uncomfortable levels. From an experimental perspective, this approach provides targeted
195 heating and eliminates some confounding factors that can arise when using other modalities
196 (such as hydrostatic effects of HWI).

197 Vardiman et al. [25] observed that microwave diathermy (40 min, 24 h before eccentric
198 knee extension exercise) significantly reduced muscle interleukin-6 (IL-6) protein content
199 compared with the control group. Microwave diathermy also blunted the increase in muscle
200 tumor necrosis factor-α (TNF-α) protein content for 72 h post-exercise.

Evans et al. [26] compared active warm-ups with low- and high-heat microwave diathermy treatments before eccentric exercise. The control group completed a high-heat passive warm-up only. The low-heat group had less proximal swelling in the belly of biceps brachii at 24 and 48 h post-exercise compared with the active warm-up group. By contrast, loss of range of motion during elbow flexion was greatest in this group. Subjects treated with high-heat showed less swelling and reported less muscle soreness (biceps brachii region) at 24 and 48 h after exercise compared with the active warm-up group. Nevertheless, caution should be applied when interpreting these data, owing to the smaller sample size (n=4) in the high-heat group compared with the low-heat group (n=10).

Saga et al. [16] found that microwave diathermy (150 W, 20 min) of one arm 24 h before eccentric exercise resulted in higher MVC force and range of motion immediately post-exercise, compared with the unheated contralateral arm. Nosaka et al. [11] used a similar microwave diathermy protocol to Saga et al. [16] (150 W, 20 min), 16–20 h before eccentric exercise of the arms. Their results also showed that post-exercise muscle soreness was lower, changes in elbow range of motion were smaller, and recovery of MVC force was faster in the heated arm compared with the non-heated, contralateral, control arm.

In contrast with these beneficial results, other human studies have reported no changes (and also detrimental effects) in response to pre-heating. Nosaka et al. [18] applied microwave diathermy (100 W, 10 min) 3 min before eccentric exercise of the forearms. Heat did not significantly improve performance or markers of recovery (including muscle soreness and plasma CK activity). The treatment also reduced elbow range of motion after exercise. Castellani et al. [27] applied microwave diathermy (100 W, 15 min) immediately before eccentric exercise of the elbow flexors. This treatment did not influence markers of muscle damage such as MVC force, elbow range of motion, and plasma CK activity. The only

225 significant change was an increase in plasma HSP70 concentration at 120 h post-exercise for
226 the heat group.

227 Symons et al. [15] applied 10 min of ultrasound to biceps brachii immediately before
228 baseline tests, and subsequent eccentric exercise of the elbow flexors. They observed no effects
229 of ultrasound on muscle soreness, isometric strength and elbow range of motion. The authors
230 stated that muscle temperature did not increase as expected (~1.8°C increase versus expected
231 increase of ~3.5°C), which may have altered the responses to heating.

232 Different approaches to heating may account for some of these variable findings. The
233 intensity of microwave diathermy may influence its effectiveness. Nosaka et al. [11] expected
234 that microwave diathermy treatment would raise muscle temperature to ~41°C, based on pilot
235 work. The authors used microwave diathermy at 150 W for 20 min, with the probe of the
236 diathermy unit placed 15 cm away from the mid-portion of the biceps brachii. This protocol
237 differed from that used in their earlier study [18], which involved 100 W for 10 min duration,
238 with the probe placed 5 cm away from the upper arm (specific location not stated). Castellani
239 et al. [27] also used microwave diathermy at 100 W for 10 min immediately before exercise,
240 and found no effect on markers of muscle damage. Compared with pre-heating at 100 W [18],
241 pre-heating at 150 W [11] caused a greater increase in muscle temperature (increase of ~7°C
242 after 150 W treatment versus ~3.5°C after 100 W treatment). This greater rise in muscle
243 temperature may account for the beneficial effects reported by Nosaka et al. [11] (i.e., reduced
244 muscle soreness and improved range of motion in the heat group).

245 The timing of microwave diathermy before exercise may also influence its effectiveness.
246 Nosaka et al. [11] heated muscle ~19 h before exercise, while Saga et al. [16] heated muscle
247 24 h before exercise. By contrast, Nosaka et al. [18] and Castellani et al. [27] heated muscle
248 immediately before exercise. There were greater benefits of heating 19 to 24 h before exercise

[11, 16] compared with heating immediately before exercise [18, 27]. Therefore, to generate any benefit, pre-heating may need to occur >16 h before exercise, and result in a high core and/or muscle temperature.

2.3.2 Post-Heating

Animal and human studies have also been conducted to examine the effects of post-heating, using several different heating methods. Table 2 highlights the post-heating literature.

2.3.2.1 Animal Studies.

An extensive amount of research exists on the effects of heating after exercise or injury. Takeuchi et al. [5] induced a crush injury to muscle in rats before heat (42°C water in a plastic bag) was applied to the injured site for 20 min. Muscle inflammation and regeneration was examined over 28 d post-injury. Macrophage infiltration, expression of insulin-like growth factor-1, and proliferation of Pax-7+ satellite cells in injured muscle occurred more rapidly in the heat-treated rats compared with non-heated control rats. These effects were accompanied by a greater number and size of regenerating muscle fibres at 2 d, and fewer collagen fibres at 14 and 28 d post-injury in heat-treated rats compared with non-heated control rats. In a similar study, Shibaguchi et al. [28] injected rat hind limbs with bupivacaine to induce muscle injury, and then treated the rats with heat (HWI, 42°C, 30 min, 2 d after injury and on alternate days during 14 d of recovery). Their results indicated that soleus muscle mass (relative to body mass), myofibrillar and total protein content, and muscle fibre size at 28 d post-injury were all not significantly different compared with non-heated rats. Nevertheless, heat treatment did restrict the deposition of collagen fibres, and increased Pax-7+ satellite cells in muscle compared with ice treatment.

The study by Kojima et al. [22], described in section 2.3.1.1, also investigated the effects of heating rats in an environmental chamber after cardiotoxin or saline injection. Heat treatment increased whole muscle protein content in rats treated with saline compared with non-heated rats treated with saline, and heated rats treated with cardiotoxin at 28 d post-injury. The number of Pax-7+ satellite cells in muscle was also higher in heated rats compared with control rats 3 d post-injury.

Selsby et al. [29] used a thermal blanket to maintain core temperature between 41–41.5°C for 30 min after 6 d of hind limb immobilisation, and during a 7-d limb reloading period. Heat treatment increased muscle mass after the reloading phase compared with no treatment.

Collectively, the findings from these animal studies reveal benefits of heat treatment for expediting muscle repair/inflammation following injury, and helping to restore muscle mass following immobilisation. In these contexts, heat treatment may have benefits for recovery following exercise and musculoskeletal injuries that require periods of rest or reduced physical activity.

2.3.2.2 Human Studies.

Research from human studies using post-exercise heating has found some benefits. Clarke [30] investigated the effects of 46°C HWI and 10°C cold water immersion (CWI) on short-term recovery of handgrip strength after a single 2 min maximal handgrip contraction[30]. HWI increased handgrip force 2 min post-exercise, compared with CWI. However, there were no other significant differences between the treatments. Mayer et al. [31] applied heat wraps for 8, 18 and 32 h after lumbar extensions (two sets, 25 reps, load of 100% peak isometric lumbar extension strength). Compared with cold packs (control group), heat wraps provided greater pain relief at 24 h, and greater satisfaction with the treatment. Another group of subjects applied heat wraps to the lumbar spine ~4 h before and for 8 h after exercise. Heat-treated subjects

296 reported less pain, and fewer changes in self-reported physical function and disability
297 compared with the control group at 24 h.

298 Several studies have examined the effects of HWI and warm water immersion on exercise
299 performance and recovery from muscle damage. Viitasalo et al. [32] examined the effects of
300 warm water immersion (36.7–37.2°C, 20 min) with underwater jet massage on strength and
301 power performance measures, and blood markers of muscle damage, such as myoglobin, CK
302 and lactate dehydrogenase. Track and field athletes from various disciplines completed warm
303 water immersion 20–30 min after each of the five training sessions (strength training, jumping
304 training, speed training and sport specific training) during a 3-d training week. Warm water
305 immersion attenuated the decrease in jump power, and limited the increase in ground contact
306 time from five successive rebound jumps compared with the control group. Warm water
307 immersion did not influence markers of muscle damage, or muscle soreness measures.

308 Kuligowski et al. [33] used a heated whirlpool protocol (38.9°C, 24 min, arm immersed to
309 mid-deltoid level) to examine the effects on the recovery of range of motion, muscle soreness
310 and MVC force after one bout of eccentric exercise of the elbow flexors. Whirlpool therapy
311 was conducted immediately after, and 24, 48 and 72 h after exercise. Compared with no
312 treatment, this type of heating restored relaxed elbow flexion angle more rapidly. There were
313 no significant effects on perceptions of muscle soreness, recovery of strength, or active elbow
314 flexion and extension.

315 Two HWI studies were conducted by Vaile et al. [8, 9]. HWI was applied during 5
316 consecutive days of cycling [9] or immediately after, and every 24 h up to 72 h after an
317 eccentric leg press protocol [8]. The HWI protocol was identical in both studies (38°C for 14
318 min, immersion of whole body excluding head and neck). HWI was no more effective than
319 passive recovery and CWI for maintaining cycling performance over 5 d [9]. However, heart

rate following time trials on days 2–5 tended to be lower (effect size > 0.6) after HWI compared with passive recovery. In their other study, Vaile et al. [8] found that HWI significantly attenuated the decrease in isometric squat force at 24, 48 and 72 h following an eccentric leg press protocol. HWI also reduced plasma CK activity 48 h post-exercise compared with passive recovery. HWI did not influence recovery of weighted squat jump performance, mid-thigh girth, or other blood markers of muscle damage and inflammation.

Finally, Pournot et al. [22] used warm water immersion (36°C, 15 min, sitting depth to iliac crest) after two bouts of intermittent rowing, separated by 10 min. HWI did not attenuate losses in MVC force and counter movement jump height at 1 and 24 hrs, or mean power during a 30-s all-out rowing sprint performed at 1 h after exercise. HWI also failed to reduce plasma CK activity, lactate concentration, and blood leukocyte count at 24 h after exercise.

Other modes of post-exercise heat therapy include heat pads. Jayaraman et al. [34] had participants complete a single-leg knee extension eccentric exercise program (involving completing sets to failure before reducing weight and repeating). Participants then underwent one of the following treatments: (1) application of a heat pad at 41°C for 2 h; (2) a short warm-up of the treatment leg before completing six static stretches; (3) heat pad and stretching, or (4) no treatment (control), with recovery strategies completed at the same time every day until muscle soreness had subsided. Magnetic resonance imaging (to determine edema), isometric strength of the quadriceps, and pain were measured periodically over the days post-exercise. No differences existed between conditions for muscle soreness, recovery of strength or T2 relaxation times (as an indication of edema).

The varied exercise protocols used in the studies above make it challenging to summarise the effects of post-exercise heating. In most studies, temperature was in the range of 36–39°C (one study using 46°C [30]), and the period of HWI varied from 10–24 min. Exercise protocols

included eccentric exercise [8, 33], intermittent activity [35] or consecutive days training [9, 32]. This variability makes it difficult to compare studies and arrive at any definitive conclusions about the potential benefits of heat after exercise or injury in humans. For example, there is some variability in the responses of CK to HWI/warm water immersion treatment. Viitasalo et al. [32], Pournot et al. [35] and Vaile et al. [8] all showed no benefit of warm water immersion and HWI (respectively) on plasma CK activity or lactate dehydrogenase concentration 24 h post-exercise. However, Vaile et al. [8] did find a reduction in plasma CK activity at 48 h in the HWI condition. In contrast, Viitasalo et al. [32] did not observe any such effect at approximately 36 h post training. Measuring CK at 24 h post-exercise in the study by Pournot et al [35] was also possibly too early to detect any change. Substantial differences between the exercise models used by Vaile et al. [8] and Viitasalo et al. [32] make it difficult to determine whether HWI and warm water immersion (respectively) may reduce CK responses ≥48 h post exercise. As Vaile et al. [8] showed, HWI attenuated the loss in isometric squat performance, and reduced plasma CK activity, but it did not improve recovery of weighted jump squat performance. When examining the effect of heat on markers of muscle damage, it is therefore important to assess a wide range of markers. Finally, the use of heat during a training block make it difficult to determine which specific application of the heat therapy contributes to the beneficial outcomes. For example, Vaile et al. [9] used HWI after each training session of a 5-d training block. Therefore, the HWI used after days 1–4 could be considered as pre-heating for the following days' (i.e. days 2–5) training session. This approach contrasts with another study by Vaile et al. [8], in which they applied HWI after one eccentric exercise protocol. Multiple exposures of heat therapy on consecutive days may also lead to heat acclimation, which may limit any potential beneficial effects. This further confounds comparisons of post-exercise heating.

2.3.2.3 *Summary*

Post-exercise/injury heat has shown some significant beneficial effects in animal models, however heating in humans has produced mixed results. Systematic human trials are required that compare different water temperatures, types of exercise protocols, and the timing of HWI/warm water immersion application to determine the most beneficial recovery protocol.

2.3.3 Heat During Experimental Treatment

A paucity of research has investigated the effects of heat treatments during exercise, normal daily activity and muscle atrophy. Nevertheless, some benefits have been reported, as described in detail in Table 3.

In a rat model, Morimoto et al. [3] injected rats with dexamethasone 6 d/wk for 2 wks to induce muscle myopathy. In conjunction with the injections, a group of rats were heat treated (HWI, 42°C, 60 min, hind limbs immersed, once every 3 d for 2 wks). Heat treated and dexamethasone, and dexamethasone-only rats were compared with a control group (saline injections). The diameter of type I, type IIa and type IIb muscle fibres in the heated group was greater compared with the non-heated group, indicating that heating attenuated muscle atrophy associated with dexamethasone treatment. Further investigation of the mechanisms for this effect revealed that heat treatment attenuated messenger RNA (mRNA) expression of the atrogenes muscle ring finger (MuRF1) and atrogin-1 compared with the non-heated rats.

Selsby and Dodd [6] applied heat during rat hind limb immobilization to induce muscle atrophy. A thermal blanket was used to maintain core temperature at 41–41.5°C for 30 min. This treatment was applied 24 h before immobilization, and on alternate days during immobilization. Heat treatment attenuated muscle atrophy (as measured by soleus mass) and oxidative damage in muscle (as measured by 4-hydroxy-2-nonenol and nitrotyrosine).

Goto et al. examined the effects of heating during training [4] and the use of heating during day-to-day activity in humans [2]. In their training study [10], they found increases in muscle cross sectional area and strength when heating (heat and steam sheets, 30 min before and during the 30 min exercise sessions) was applied during a 10-wk low-intensity training program. Although the heating was applied during the exercise in this study, heat was also applied before the exercise commenced. It is therefore difficult to determine if the results of the study were due to the heating before or during the exercise. The arm selected for heating was the non-dominant arm, and gains in muscle mass in this arm were greater than in the non-heated, dominant arm. This outcome makes it difficult to determine if the increase in muscle mass in the heated, non-dominant arm was due to heating, or increased (unaccustomed) use of the non-dominant arm during training.

In another study by Goto et al. [2], participants applied heat (heat and steam sheets, upper leg, 8 h per day) without any formal exercise training for 10 wks. One leg was randomly chosen to receive the treatment, with the contralateral leg serving as control. Heat treatment increased cross-sectional area of the vastus lateralis, rectus femoris and quadriceps (taken as a whole), and increased maximum isometric torque. Although the participants were instructed not to complete any exercise training during the 10 wk period, the differences in daily activities during the times when heating was applied (or when it was not) may have influenced the results.

However, in comparison to the studies by Goto et al. [2, 10], Stadnyk et al. [36] found no benefit of heat. Untrained participants completed 30 sessions of resistance exercise over 12 weeks (2-3 sessions/wk). Participants completed 4 sets of 8 repetitions at a weight equal to 70% 1-RM, with both concentric and eccentric contractions of knee extensors completed in each session. Heat pads (that increased muscle temperature to 38°C) were applied during and 20 min after each session to a randomly selected leg with the contralateral leg acting as the control. Whilst both legs significantly increased muscle mass, peak and mean concentric

torque, peak rate of force development and 3-RM knee extension, there were no significant differences between the heated and control legs. Considering heat was applied during and after the exercise session in the current study, compared to before and during the exercise session in Goto et al. [10], this may be a key variable to induce the potential beneficial effects of heating on exercise induced adaptations.

Further research is needed in this area, with more tightly controlled studies to understand the potential of using heat during exercise to improve performance, adaptation and/or assist with recovery, as the studies completed to date have some limitations, as described above.

3. MOLECULAR MECHANISMS RESULTING FROM HEATING

Evidence suggests that heat elicits protective effects that attenuate muscle injury and performance decrements, and enhance therapeutic effects that assist recovery and adaptation. Some of the purported mechanisms governing these effects involve HSPs, kinases in the mTOR pathway, and genes associated with muscle hypertrophy/atrophy.

3.1 HSPs

HSPs are proteins that respond to stress within the body. They are classified numerically by their molecular weight, from HSP10 at 10 kDa to HSP110 at 110 kDa. HSPs have a number of functional roles, including cell chaperoning, preventing protein denaturation and aggregation of cellular located proteins [37], cell protection from stressors, cell signalling [38] and maintaining cell homeostasis [39]. HSP expression increases in response to various stressors, including hypoxia and protein degradation [38]. HSPs may also play important specific roles in combating the onset and progression of certain medical conditions. As discussed in the review by Archer et al. [40], HSP72 increases to help prevent the development

of insulin resistance, whereas prolonged consumption of a high-fat diet suppresses HSP72 expression. Thakur et al. [41] also discussed the potential for HSP72 to attenuate disease progression in muscular dystrophy. HSPs therefore respond to and mediate a wide and diverse range of stressors. Considering that heating and exercise both induce stress on the body, it is logical to expect that both stimuli would increase HSP expression. However, contrasting research exists.

HSP expression increases after heat and mechanical stress on muscle cells [42]. In this particular study, rat myoblast cells were exposed to one of four conditions: (1) 97 h at 37°C (control condition); (2) heating at 41°C for 1 h, then maintenance at 37°C for 96 h; (3) mechanical stretching at 37°C for 1 h, then 96 h of mechanical stretching at 37°C, and (4) heating and stretching at 41°C for 1 h, then 96 h of mechanical stretching at 37°C. Cell HSP72 and HSP90 expression increased in all conditions except the control condition. Maglara et al. [43], found that heat (incubation at 42°C, 30 min) increased HSP25 (at 4 and 18 h post-heating) and HSP60 (12 and 24 h post-heating) and heat shock cognate 70 (at 8, 12, 18, 24 h post-heating) in myotubes compared with no heating. Other muscle cell culture studies also report that heat stress (41°C for 1 h) increased HSP72 expression, blocked dexamethasone-induced decreases in HSP72 expression [44], and suppressed nuclear factor κB (NFκB) activation [45].

Shibaguchi et al. [28] examined the effects of heating in rats (HWI, 42°C, 30 min) 2 d after bupivacaine injection (to induce muscle injury), and on alternate days during 14 d of recovery. They observed a transient rise in HSP72 expression in muscle 3 d after muscle injury compared with non-heated rats. Garramone et al. [20] found that HSP72 was only present in the gastrocnemius of rats that were heat treated (HWI, core temperatures maintained at 42.5°C for 20 min) 12 h before lower limb ischemia. In immobilised rats, Selsby and Dodd [6] discovered that maintaining core temperature between 41–41.5°C for 30 min with a heat blanket increased

464 muscle HSP25 expression by 75%, and HSP72 expression by 7-fold. There were no changes
465 in HSP expression in the control group (immobilisation only). In another rat study, Morimoto
466 et al. [3] showed a significant increase in muscle expression (extensor digitorum longus) of
467 HSP72 in heat-treated rats (HWI, 42°C, 60 min, hind limbs immersed, once every 3 d for 2
468 wks) after undergoing 2 wks of dexamethasone treatment. Touchberry et al. [17] also reported
469 that heating 48 h before eccentric exercise raised HSP72 expression in muscle of rats compared
470 with an eccentric exercise only group. Kojima et al. [22] observed an increase in HSP72
471 expression in rats that received heat treatment before or after a saline injection compared to
472 non-heated saline controls at 3 and 7 d post-injection. Frier and Locke [7] heated rats before
473 muscle overload (through removing the gastrocnemius muscle) and discovered that HSP72 and
474 HSP25 expression increased in muscle. As demonstrated in these animal studies, HSP
475 expression increases with heat application and may be a contributing factor to the beneficial
476 effects generated from heating.

477 Human investigations have also reported that heating increases HSP expression in muscle.
478 Ogura et al. [46] demonstrated an upregulation of HSP27, 72 and 90 expressions in muscle 24
479 h after microwave diathermy, which increased muscle temperature at 2 cm depth to ~40°C at
480 the end of the heat treatment. Castellani et al. [27] applied microwave diathermy (100 W, 15
481 min) immediately before eccentric exercise of the elbow flexors and found an increase in
482 plasma HSP70 at 120 h post-exercise. Touchberry et al. [47] found a significant increase in
483 muscle HSP70 and HSP27 phosphorylation in muscle 24 h after 20 min microwave diathermy
484 and 20 min heat pack application. This HSP increase, however, was only found in female
485 subjects. These same subjects also had higher basal expression of HSP70 before the
486 intervention, which may have confounded these findings. In a recent human study [48], heating
487 the leg with a water perfused suit (48–52°C, 90 min) increased the expression of several genes
488 in muscle, including those encoding HSPs (Figure 3).

Morton et al. [49] used HWI to induce HSP expression in human muscle. One leg was heated, while the contralateral leg served as a control. Muscle biopsies were performed pre-immersion, and then at 2 d and 7 d afterwards. Immersion raised muscle temperature to 39.5 ± 0.2 °C at 3 cm depth, similar to muscle temperatures after exercise [50]. However, HWI did not alter the expression of HSP27, 60, or 70. The authors concluded that HSP expression in muscle may depend on factors other than heat. Differences in heating methods and sampling times may explain the observed disparity between these findings and those described in the previous paragraph.

The induction of HSPs may account for some of the benefits of heating (including faster recovery of MVC force and attenuation in loss of range of motion [11]), because the HSPs protect cells from damage [37, 51]. In the studies reviewed above that reported increased HSP expression from heating, also reported benefits to muscle including increased protein content [22, 42], increased cross sectional area [28] and increased muscle regeneration [4]. Nevertheless, considering the equivocal findings described above, more systematic and well controlled research is needed to clarify the effects of heat on HSP expression in muscle. Additional research is also required comparing the effects of different heating modalities on HSP expression.

3.2 mTOR kinases

Activation of kinases up- and downstream of mTOR stimulates cell growth and proliferation, and influences muscle hypertrophy [52, 53]. The activity of mTOR-related kinases increases after strength and hypertrophy exercise, and decreases during detraining [54]. For example, ribosomal protein S6 kinase (p70S6K) (downstream target of mTOR) contributes to muscle growth during early postnatal life in rats, and the phosphorylation of p70S6K

decreases in young adult rats [55]. Phosphorylation of protein kinase B (Akt) (upstream of mTOR) increases during periods of muscular overload. Finally, eukaryotic translation initiation factor 4E-binding protein 1 (4E-BP1) (down-stream of mTOR) may influence cell size in mammals [55]. Induction of rapamycin can block targets down-stream of mTOR leading to decrease muscle mass, so these kinases are important contributors to muscle hypertrophy [55]. Research from animal and human models into the muscular effects of heat has also examined these kinases.

Yoshihara et al. [56] exposed rats to one of five different heat environments (37, 38, 39, 40 or 41°C HWI), or a control condition without heat stress. Soleus and plantaris muscles were removed immediately after the heat exposure. Compared with no heat stress, phosphorylation of the upstream regulator of mTOR, Akt (Ser473) [57], was increased after 40 and 41°C HWI in the soleus muscle, and after 39, 40 and 41°C HWI in the plantaris muscle. After 41°C HWI, Akt phosphorylation was higher in the soleus muscle (compared with 37, 38 and 39°C) and in the plantaris muscle (compared with 37°C). Phosphorylation of p70S6K (Thr389) was also significantly greater in the soleus muscle after 41°C (versus no heat, 37 and 38°C), and in the plantaris muscle (versus no heat and 37°C). However, the expression of another kinase downstream of mTOR, 4E-BP1 (Thr37/46), was similar between the different treatment groups.

Finally, Kakigi et al. [58] used microwave diathermy (150 W) for 20 min immediately before isokinetic knee extension exercise in humans. Muscle biopsies were collected pre-heating, immediately post-exercise, and 1 h post-exercise. Heat significantly increased phosphorylation of Akt (Ser473), mTOR (Ser2448) and ribosomal protein s6 (S6) (Ser235/236) at 1 h post-exercise compared with no heat treatment. p38 mitogen-activated protein kinase (p38 MAPK) phosphorylation (Thr80/Tyr182) was increased immediately post-exercise with

heating compared with no heating. Finally, heat treatment increased phosphorylation of 4E-BP1 (Thr37/46) at 1 h compared with post-exercise values.

There is an important link between mTOR and HSPs. Chou et al. [59] conducted a series of studies evaluating this relationship. In HeLa cells, mTOR knockdown reduced cell survival and substantially reduced expression of *Hsp70*, *Hsp90,* and *Hsp110* genes. mTOR knockdown also inhibited phosphorylation of heat shock transcription factor 1 (HSF1) serine 326, which most likely accounted for the reduced expression of HSP genes. Finally, mTOR inhibition (by rapamycin) and knockdown suppressed activation of the *hsp70.1* promoter. These results show the importance of mTOR for HSP expression.

In summary, the mTOR pathway plays an important role in the process of muscle anabolism and regeneration, and in the heat shock protein response. Altering muscle temperatures for optimal activation of the mTOR-associated kinases could contribute to the improvements in muscle mass following regular heat treatment, with or without strength training [2, 10].

3.3 Effects of heat on other molecular mechanisms of muscle growth and atrophy

Research has also investigated the effects of heat on other molecular mechanisms for muscle growth and atrophy. Maglara et al. [43] heated mouse myotubes (42°C incubation, 30 min) and exposed them to a calcium ionophore (A23187) or a mitochondrial uncoupler (2,4-dinitrophenol) to induce cell damage. Heat treatment reduced CK activity in the myotubes following exposure to both A23187 and 2,4-dinitrophenol. Guo et al. [60] cultured C2C12 muscle cells at 37, 39 or 41°C for 24–120 h. Compared with cells cultured at 37°C, myotube width and length increased to a greater extent and more rapidly under culture at 39°C. By contrast, myotube width and length were diminished in cells cultured at 41°C. Analysis of gene

560 expression revealed that cells cultured at 39 and 41°C possessed increased expression of genes
561 involved in myogenesis (e.g., myogenic factor 5, myogenic differentiation 1),
562 myofibrillogenesis (e.g., nebulin, titin, MHC 1, MHC 2) muscle hypertrophy (e.g., α1- and β2-
563 adrenergic receptor; Akt1 and Akt2) and atrophy (e.g., calpain 2, F-Box only protein 32,
564 forkhead box protein O1 (FoxO1), forkhead box protein O3 (FoxO3)) versus cells cultured at
565 37°C (Figure 3). In another recent study, Tsuchida et al. [44] cultured C2C12 myotubes at 37
566 or 41°C for 60 min, 6 h prior to treating the cells with dexamethasone. Compared with
567 incubation at 37°C, incubation at 41°C suppressed dexamethasone-induced decreases in
568 myotube diameter and myofibrillar protein content. Heat stress attenuated these atrophic effects
569 by blocking dexamethasone-induced decreases in the phosphorylation of Akt (Thr308),
570 glycogen synthases kinase 3 beta (Ser9) and p70S6K (Thr389), and blocking dexamethasone-
571 induced increases in the mRNA expression of regulated in development and DNA damage
572 responses (REDD) 1, Kruppel-like factor 15 and MuRF1 (but not atrogin-1), and the
573 phosphorylation of FoxO1 (Ser256) and FoxO3 (Ser253). Luo et al. [61] also reported that
574 compared with incubation of L6 myotubes at 37°C, incubation at 43°C for 1 h prevented
575 dexamethasone-induced protein degradation by maintaining NFκB DNA binding activity.

576 These findings offer detailed evidence that heating can promote muscle cell differentiation
577 and alter the expression of various genes, kinases and transcription factors involved in muscle
578 remodelling. However, the effects of heat on muscle cells appear to depend on temperature and
579 the period of exposure to heat [60].

580

581 **3.4 Effects of heat on inflammation and oxidative damage**

As discussed previously in sections 2.3.1.1, 2.3.2.1 and 2.3.3, heat has elicited some beneficial effects on markers of inflammation and oxidative damage after muscle injury. Selsby and Dodd [6] immobilized the hindlimbs of rats, and applied heat during the immobilization to one group of rats. Heat attenuated increases in 4-hydroxy-2-nonel and nitrotyrosine compared with a control group of rats that were immobilized without heating. In another study, Selby et al. [29]reported that heating applied during a period of reloading (after hindlimb immobilization) also attenuated oxidative damage (as determined by reductions in 4-hydroxy-2-nonel and nitrotyrosine). Finally, Naito et al. [62] incubated human muscle samples in an organ bath at 42°C or 37°C while simultaneously exposing the samples to H_2O_2. Compared with 37°C, incubation at 42°C reduced lipid peroxidation and damage to mitochondria following H_2O_2 exposure. Regarding the effects of heat on inflammation in muscle, Takeuchi et al. [5] reported earlier infiltration of macrophages in muscle of rats that were treated with heat after muscle injury compared with rats that were not heat treated. In turn, this effect appeared to promote faster muscle fibre regeneration. In humans, Vardiman et al. [25] reported that microwave diathermy before and eccentric exercise protocol, reduced intramuscular IL-6 and prevented increases in intramuscular TNF-α. However, Castellani et al. [27] found no influence of heat on plasma IL-10 IL-1β and IL-6. In summary, heat may limit oxidative damage, but further investigations into the influence of heat on inflammatory outcomes are needed.

4. TECHNICAL CONSIDERATIONS

One commonly reported variable when using heat treatment is the change in muscle temperature. Although the various heat treatments can increase muscle temperature, variations in methods of temperature assessment make it difficult to compare studies. For example, some studies reported that muscle temperature was measured at a depth below the skin surface,

606 whereas others have reported the depth of temperature assessment within the muscle belly
607 itself. Without reporting subcutaneous fat mass, comparing studies utilising the same
608 temperatures/intensity of heating is difficult.

609 Additionally, few human exercise trials have reported muscle temperatures during
610 experimental sessions. In most studies, temperature was not measured, or it was estimated from
611 pilot work or previous studies. The common reason for not measuring muscle temperature is
612 that the invasive nature of this procedure may affect the ability of participants to exercise.
613 Although this is a genuine issue, it does make it difficult to compare studies if (perhaps) the
614 temperature of the muscle did not change as expected. For example, Symons et al. [15] used
615 ultrasound to induce heating, with a predicted increase in muscle temperature of ~3.5°C (based
616 upon other published work). However, the actual increase in muscle temperature was only
617 ~1.8°C, which could account for the absence of any differences identified between heat
618 treatment and control trials. Measuring muscle temperature, if possible, is therefore a key
619 aspect of understanding the physiological effects of heat.

620

621 **5. CONCLUSIONS AND FUTURE RECOMMENDATIONS**

622 Studies have demonstrated that heat can assist with recovery, performance and adaptation
623 to exercise, potentially by increasing the expression of HSPs to protect cells from
624 stress/damage, upregulating/downregulating pathways and genes associated with muscle
625 hypertrophy/atrophy, respectively. Several conclusions can be drawn from heat research to
626 date. First, increasing muscle temperature to approximately 40°C may be necessary to induce
627 beneficial effects on muscle. In rats, Yoshihara et al. [56] found that activation of the kinases
628 associated with mTOR was heat-dependent, with greater phosphorylation of Akt occurring at
629 higher temperatures. Additionally, Ogura et al. [46] demonstrated increases in HSP expression

in humans after muscle temperature rose to approximately 40°C. Second, heating >16 h before exercise/stress seems to produce beneficial results compared with heating immediately before exercise/stress (possibly through increased expression of HSPs, because HSPs are known to increase in humans ~24 h after heating). However, heating during activity also seems to provide beneficial effects [2, 10, 11, 18]. More human trials utilising heat and exercise sessions or training blocks should be conducted to gauge the potential benefits of heating, and determine the realistic potential for this therapy for the general population and elite athletes.

Some recommendations for further investigation into heating strategies are as follows.

- Research to date has demonstrated that the benefits for HWI are small or non-existent when using water temperatures at approximately 38°C. Considering that other forms of heating (e.g., microwave diathermy, environmental chamber) have demonstrated benefits for performance and recovery, HWI methodology may need to be reviewed. HWI at higher temperatures and/or for longer periods might be needed to stimulate the appropriate processes to enhance recovery, performance and adaptation.
- Because heat can regulate kinases up- and downstream of mTOR, and various genes involved in muscle remodelling, heat may also confer some advantages for maintaining muscle protein synthesis and muscle mass in the elderly or in people suffering from muscle-wasting disorders. The age-associated process of sarcopenia can increase the risk of falls [63]. The use of heat in conjunction with strength training in the older population may help to slow the progress of sarcopenia, thereby helping to maintain functional status [63].
- Most of the human studies to date have examined the effects of heating after exercise-induced muscle damage. This damage is not as severe as that resulting from muscle

tears or ruptures. More research is needed to determine whether heating helps to promote recovery from severe muscle injuries.

- Heat treatment in conjunction with limb immobilisation may have some clinical benefits in the context of rehabilitation. Several animal models have demonstrated the potential for using heating during immobilization in humans. The benefits, such as a more rapid return to work/sport, are substantial, and therefore warrant future investigation.
- As described in this review, there is wide variation in the types and timing of heat treatments in humans. Future research could compare the type and timing of heat treatment in a more systematic fashion. This approach may help to determine the most effective heat treatment options in individual sporting or clinical settings.

Table 1. Summary of pre-heating studies				
Pre-heating: Animal				
Reference	**Heating method**	**Stress/exercise**	**Advantages for heat group/s**	**Disadvantages for heat group/s**
Garramone et al. [20]	HWI, core temperature maintained at 42.5°C for 20 mins, 12 h before ischemia.	Ischemia of the lower limb for 90 mins.	Increased creatine phosphate in heat group vs. control.	N/A
Touchberry et al. [17]	HWI, 43°C, core temperature maintained 41-41.5°C, 20 min, 48 h before exercise.	Downhill running, 5 min bouts, 2 min rest (90 min total).	Lower CK at 2 h post. Increased expression of MHC neo at 2 and 48 h post-exercise. Increased muscle protein content at 48 h.	Less immune cell infiltration at 48 h compared to exercise only group.
Naito et al. [21]	EC, 41°C, 60 min, 6 h before hind limb suspension.	Hind limb suspension for 8 d.	Less muscle loss compared to control group. Higher total myofibrillar and soluble protein content than control.	N/A
Kojima et al. [22]	EC, 41°C, 60 min, 24 h before stress.	Injection of cardiotoxin (venom from Chinese cobra) to stimulate muscle necrosis-regeneration cycle.	Non-significantly higher protein content in heat-treated and saline injected rats vs. control (no heat/stress). Increased protein content in heated and stressed rats vs. stressed only.	N/A
Uehara et al. [64]	EC, 41°C, 60 min before soleus removal at 1, 7 and 14 d post heating	N/A	Greater muscle mass to weight ratio, increased cell proliferation and phosphorylation of p70S6K compared to control.	N/A
Frier and Locke [7]	HP, maintain core temp maintained 42°C for 15 min, 24 h before gastrocnemius removal to include overload	Overload via removal of gastrocnemius in one leg.	N/A	Less increase in total muscle protein (plantaris) and less expression of type I MHC protein.
Pre-heating; Human				
Iguchi and Shields [12]	EC, 73°C, 30 min before exercise	Fatigue task of elbow flexors.	Greater muscle relaxation rate following MVC.	N/A
Khamwong et al. [23]	HoP, stored in 75°C water for 2 h, 20 min, exercise completed 5 min after.	Eccentric contractions of wrist extensors. 5 sets, 60 reps, 1 min between sets.	Less deficit in pain threshold for whole study period, at muscle origin site at 2 d and muscle site at 3 d. Less deficit in passive flexion ROM, passive extension ROM and	N/A

			active extension over whole study period and passive flexion ROM d 1-8 passive extension ROM d 2-3 and active extension on d 1-4.	
Khamwong et al. [24]	Sauna, seated, 76.6-82.2°C, 15-30% humidity for 15 min. Competed prior to exercise.	Eccentric contractions of wrist extensors. 5 sets, 60 reps, 1 min between sets.	Less deficit in passive flexion ROM d 1-7 post exercise. Less deficit in passive extension ROM 1-2 d post-ex. Less deficit in grip strength (1-2 d) and wrist extensor strength (1-3 d).	N/A
Skurvydas et al. [13]	HWI 44°C, 45 min, waist high, immediately before post-warming testing (followed by exercise task).	Drop jumps into maximal jumps. 3 sets of 10, 40 and 50 reps. Drop height of 0.5 m followed by 90° knee angle into maximal jump.	Increased jump height (% change from baseline) after 1st set and less % change at 48 hrs post-exercise compared to control. Less deficit in MVC at 48 hrs post-exercise. Smaller increase in P100 long muscle length to short muscle length ratio after 2nd and 3rd sets. Less CK and soreness at 24 and 48 hrs post exercise.	N/A
Vardiman et al. [25]	MD, 40 min, 24 h before exercise task.	Eccentric leg extensions at 120% of concentric contraction 1-RM (measured immediately before exercise task). 7 sets, 10 reps, 2 min rest between sets.	Lower IL-6 levels from baseline to 72 h (control group no difference). TNF-α did not significantly change in heat group (whereas significant increase in control group).	N/A
Evans et al. [26]	MD, 10 min before eccentric exercise. Low heat group and high heat group.	50 maximal eccentric contractions of elbow flexors.	Less swelling in low-heat group vs. active recovery. Less swelling and muscle soreness for high heat group vs. active recovery.	Lower range of motion for low-heat group at most time points for all groups.
Saga et al. [16]	MD, 150 W, 20 min, 24 h before eccentric exercise.	24 maximal isokinetic contractions of elbow flexors.	Greater MVC and ROM following eccentric exercise.	N/A
Nosaka et al. [11]	MD, 150 W, 20 min, 16-20 h before eccentric exercise.	24 maximal eccentric contractions of elbow flexors.	Less muscle soreness and smaller loss of ROM, increased recovery of MVC.	N/A

Nosaka et al. [18]	MD, 100 W, 10 min, within 3 min before eccentric exercise.	12 maximal eccentric actions of the elbow flexors.	N/A	Smaller relaxed arm angle. Greater change in flexed angle. Change in ROM larger than control and icing group.
Castellani et al. [27]	MD, 100 W, 15 min. Immediately before eccentric exercise. Also, applied for 2 min between exercise sets.	Eccentric contraction of elbow flexors. 2 sets, 24 reps, 2 mins between sets.	Increased HSP70 at 120 h post-exercise.	N/A
Symons et al. [15]	Ultrasound, 10 min, frequency 1 MHz, intensity 1.5 W per cm^2. Conducted before baseline strength measures (which then was followed by exercise task).	Eccentric contraction of elbow flexors. 50 reps.	N/A	N/A

CK: creatine kinase, EC: environmental chamber, HoP: hot pack, HP: heat pad, HSP70: heat shock protein 70, HWI: hot water immersion, IL-6: interleukin-6, MD: microwave diathermy, MHC: myosin heavy chain, MHz: megahertz, MVC: maximal voluntary contraction, N/A: not applicable, P100: muscle contraction force when stimulated at 100 hertz, reps: repetitions, ROM: range of motion, TNF-α: tumor necrosis factor-alpha, W: watts, 1-RM:1 repetition maximum.

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Table 2: Summary of post-heating studies				
Post-heating: Animal				
Reference	**Heating method**	**Stress/exercise**	**Advantages for heat group/s**	**Disadvantages for heat group/s**
Takeuchi et al. [5]	HWI (in a plastic bag), 42°C, 20 min, 5 min after injury.	Crush injury induced to muscle belly.	Greater size and number of muscle fibres vs. control. Faster induction of macrophage infiltration, increased expression of growth factors and proliferation of Pax-7+ satellite cells.	N/A
Shibaguchi et al. [28]	HWI, 42°C, 30 min, starting 2 d post-injury and every other day afterwards for 14 d.	Injection of bupivacaine into muscle belly.	Increased recovery of muscle weight (relative to body weight) and total and myofibrillar protein content, muscle fibre size, HSP72. Less deposition of collagen. Increased expression of Pax-7+ satellite cells.	N/A
Kojima et al. [22]	EC, 41°C, 60 min, immediately after stress.	Injection of cardiotoxin (venom from Chinese cobra) to stimulate muscle necrosis-regeneration cycle.	Increased protein content for heat and saline rats compared to saline only controls. Increased Pax-7+ satellite cells in heated rats vs. control. Increased HSP72 in heated controls vs. saline only controls, and heated post-cardiotoxin injection vs. cadiotoxin only controls.	
Selsby et al. [29]	TB, maintain core temperature 41-41.5°C for 30 min, after stress and every 48 h after for 7d.	6 d of immobilization of hind limbs followed by 7 d reloading phase	Greater muscle mass during reloading phase	N/A
Post-heating; Human				
Clarke [30]	HWI, 46°C, 10 min, following exercise.	1 maximal handgrip contraction for 2 min	Greater force output at 2 min test vs. cold	N/A
Mayer et al. [31]	1. Heat wrap applied for 8 h at 18 and 32 h post-exercise task. 2. Heat wrap applied 4 h before exercise and worn for	2 sets, 25 reps at 100% peak isometric lumber extension strength. 2 min rest between sets.	1. At 24 hrs post exercise, pain relief score better than cold pack group. Higher satisfaction with outcome for heat group than cold pack group. 2. Less pain and less	N/A

	8 h total (including during exercise).		change in self-reported physical function and self-reported disability vs. control.	
Viitasalo et al. [32]	Warm water immersion, ~37°C, 20 min, 20-30 min after training session.	3 d training week.	Smaller decrease in jump power, slowed increase in contact time for 5 successive jumps.	N/A
Kuligowski et al. [33]	WP, 38.9°C, 24 min, immediately after and 24, 48 and 72 h post exercise.	5 sets, 10 reps of eccentric exercise of elbow flexors.	Greater recovery of relaxed elbow flexion angle.	N/A
Vaile et al. [9]	HWI, 38°C, 14 min, whole body (excluding head and neck), immediately following exercise.	5 consecutive days of 105 min cycling protocol (including sprints and time trial). Non-significant lower HR compared to PAS (moderate effect size).	Increased percent change in time trial performance vs. control.	Non-significant decrease in average power for sprints over the 5 d. Decrease in percent change in time trial performance vs. contrast water therapy.
Vaile et al. [8]	HWI, 38°C, 14 min, whole body (excluding head and neck), immediately following exercise, and every 24 h up to 72 h.	7 sets x 10 reps of eccentric contractions of leg press (5 sets 120% 1RM, 2 sets 100%).	Smaller decrease in isometric squat performance at 24, 48 and 72 h vs. control. Reduction in CK at 48 h vs. control.	Lower jump squat power compared to baseline at 72 h.
Pournot et al. [35]	Warm water immersion, 36°C, 15 min, depth to iliac crest (sitting).	10 min: rowing 30 s, 30 s rest, CMJ 30 s, rest 30 s (repeat). Two bouts separated by 10 min.	N/A	N/A

Jayaraman et al. [34]	1. HP, 41°C, 2 h, covering quadriceps muscle belly. Application start at 36 h post exercise, applied every 24 h until participant soreness subsided. 2. Heating (as described) + stretching protocol.	Eccentric knee extension. Average of 6-8 sets x 5-10 reps. Load started at 100% MVC and reduced until load was below 50% (load reduced each time participant could not achieve 5 reps in controlled manner).	N/A	N/A

CK: creatine kinase, CMJ: counter movement jump, EC: environmental chamber, HP: heat pad, HR: heart rate, HSP: heat shock protein, HWI: hot water immersion, MVC: maximal voluntary contraction, N/A: not applicable, PAS: passive recovery, reps: repetitions, TB: thermal blanket, WP: whirlpool, 1-RM: 1 repetition maximum.

Table 3: Review of heating applied during stress				
During: Animal				
Reference	**Heating method**	**Stress/exercise**	**Advantages for heat group/s**	**Disadvantages for heat group/s**
Morimoto et al. [3]	HWI, 42°C, 60 mins, hind limbs immersed, once every 3 d for 2 wk.	Dexamethasone (injected 6 d / wk for 2 wk.	Attenuation in fibre diameter and suppression of genes associated with atrophy vs. dexamethasone only group.	N/A
Selsby and Dodd [6]	TB, maintain core temperature 41-41.5°C for 30 min, 24 h before and on alternate days during stress.	Hind limb immobilization for 8 d.	Less muscle atrophy and oxidative damage vs. no treatment.	N/A
During: Human				
Goto et al. [10]	HSS, 30 min before and during 30 min of exercise. Applied to non-dominant arm (contralateral arm served as control).	3 sets x 30 reps of elbow flexion and extension, light intensity, 4 d/wk for 10 wk	Greater flexion torque of heat treated arm. Greater biceps brachii muscle mass in heated arm.	N/A
Goto et al. [2]	HSS, quadriceps of random leg, 8h/day, 4d/wk.	Worn during normal activity. (Time of day for heating not stated)	Greater isometric knee extension force in heated leg. Increased CSA in VL, RF and fibre CSA in VL in heated leg.	N/A
Stadnyk et al. [36]	HP, thigh of random leg, during and 20 mins after resistance training session.	Concentric and eccentric contractions of knee extensors. 4 sets x 8 reps at intensity of 70% of 1-RM. 2-3 d/wk for 12 wk (2-3 sessions/wk)	N/A	N/A

CSA: cross-sectional area, HP: heat pad, HSS: heat and steam sheet, N/A: not applicable, RF: rectus femoris, reps: repetitions, TB: thermal blanket, VL: vastus lateralis, W: watts, 1-RM: 1 repetition maximum.

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675 **Figure legends**

676 **Figure 1.** The whole body can be heated by sitting or exercising in an environmental
677 chamber or a sauna. Parts of the body can be heated using heat/steam sheets or immersing the
678 legs in hot water. Specific muscle groups can be heated more locally using microwave
679 diathermy. These heating methods are described and discussed in more detail in section 2.2
680 and Tables 1, 2 and 3.

681

682 **Figure 2.** Research has investigated the effects of heating on many physiological variables in
683 humans (see Tables 1, 2 and 3 for more details). The strongest and most consistent effects of
684 heating include better restoration of muscle function and less muscle soreness/swelling after
685 exercise.

686

687 **Figure 3.** Heat promotes muscle regeneration by stimulating cells and proteins involved in
688 muscle protein synthesis, and restricting muscle atrophy and fibrosis. These effects are
689 mediated (in part) by upregulation of many genes involved in muscle hypertrophy and
690 downregulation of certain genes that control muscle atrophy. See section 3 and Tables 1, 2
691 and 3 for more details. Abbreviations: Fox01, Forkhead box protein 01; HSP, heat shock
692 protein; PF4, platelet factor 4; ANGPT2, angiopoietin 2; CCL2, C-C Motif Chemokine
693 Ligand 2; VEGF, vascular endothelial growth factor; IGF1, insulin-like growth factor 1;
694 MyH1, heavy polypeptide 1 myosin; MyH1, heavy polypeptide 2 myosin; Neb, nebulin; Ttn,
695 titin; Acta 1, alpha 1 actin; Myf, myogenic regulatory factor; Myog, myogenin; Myod1,
696 MyoD; Slc2A4, Solute carrier family 2 member 4; Capn2, calpain 2; Pparg, peroxisome
697 proliferator activated receptor gamma; Adrb2, adrenoceptor beta 2; Akt2, Akt kinase 2;
698 Prkag3, protein kinase adenosine monophosphate kinase-activated non-catalytic subunit
699 gamma 3; Prkab2, protein kinase adenosine monophosphate kinase-activated non-catalytic
700 subunit beta 2; Fbxo32, F-box protein 32;

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Compliance with Ethical Standards

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Conflicts of Interest

Hamish McGorm, Llion Roberts, Jeff Coombes and Jonathan Peake declare that they have no conflicts of interest relevant to the content of this review.

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