Cross-adaptation/tolerance symposia

Accompanying video: https://youtu.be/PRTjSw07-sA

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Cross adaptation is the process of inducing physiological adaptation utilising one environmental stressor (e.g. heat) prior to exposure in another environmental stressor (e.g. hypoxia) resulting in attenuated disruption to homeostasis relative to the unadapted state (Ely *et al*., 2014; White *et al*., 2014; Gibson *et al*., 2017; Lee *et al*., 2019).

Cross-, and combined adaptation between environmental stressors may be induced at rest, or during exercise in both terrestrial environments (as a cross acclimatisation model) as well as artificial environments (e.g. a cross acclimation model). Irrespective of the method induction, the underpinning adaptations are derived from cellular and molecular pathways with adaptations at this level being described as "Cross Tolerance" with heat shock proteins and hypoxia-inducible factor 1-α identified as of greatest interest (Maloyan *et al*., 2005; Shein *et al*., 2005; Horowitz, 2007; Umschweif *et al*., 2013; Ely *et al*., 2014; Salgado *et al*., 2014; Gibson *et al*., 2015, 2016; Lee *et al*., 2016; Tuttle *et al*., 2017).

Cross adaptation may take a series of formats such as i) adaptation to one stimulus provides tolerance to another e.g. cold water immersion improves responses in hypoxia (Lunt *et al*., 2010), or heat adaptation improves exercise capacity in temperate conditions (Scoon *et al*., 2007; Stanley *et al*., 2015; Zurawlew *et al*., 2015), ii) Adaptation to two combined stimuli, provide enhanced tolerance to a third stressor e.g. exercise and heat stress enhances cardiac mechanics (Levi *et al*., 1993; Pollak *et al*., 2017) or sub-maximal/maximal exercise performance in hypoxia (Gibson *et al*., 2015; Lee *et al*., 2016; White *et al*., 2016; Sotiridis, Debevec, Ciuha, *et al*., 2018; Salgado *et al*., 2020), iii) Adaptation to one stressor, enhances adaptation to another e.g. examining whether heat or cold adaptation enhances training quality at altitude (Lee *et al*., 2019).

Multiple stressors can be experienced simultaneously, for example exercise and heat, cold and hypoxia and in some popular training locations, heat and hypoxia; combinations that may benefit many sought after indices of adaptation. The first study to employ a combined stressor (heat & hypoxia) acclimation protocol was promising a "conditioning cocktail for team-sport athletes exercising at sea level in temperate conditions" (Buchheit *et al.*, 2013). Whether the superposition of hypoxic acclimation will add to the gains observed following heat acclimation such as enhanced exercise economy (Sotiridis, Debevec, Ciuha, *et al.*, 2018), an augmented sweating response (Lorenzo and Minson, 2010), an increased power output at the lactate threshold (Rendell *et al.*, 2017) or even an increase in total hemoglobin mass (Oberholzer *et al.*, 2019) remains unresolved. Maximal oxygen uptake remains unaltered following a 10-day combined heat and hypoxic acclimation protocol that employed the controlled-hyperthermia technique in combination with shorter (8-10 hours) (Rendell *et al.*, 2017) or longer (22 hours) (Sotiridis *et al.*, 2019) daily hypoxic doses. Interestingly, indices of aerobic performance have been shown to increase in some (Buchheit *et al.*, 2013; Rendell *et al.*, 2017; Sotiridis *et al.*, 2019) but not all (McCleave *et al.*, 2017) recent studies that investigated the ergogenic potential of the combined heat and hypoxic acclimation.

The incorporation of exercise sessions into acclimation protocols renders it difficult to distinguish the effect of physiological adaptation to the environmental stressor under investigation from that of the exercise training per se (Sotiridis, Debevec, Ciuha, *et al.*, 2018; Sotiridis, Debevec, McDonnell, *et al.*, 2018; Sotiridis *et al.*, 2019). Whereas untrained individuals might improve their aerobic capacity, thermoregulatory gains are expected in trained individuals that experience a sufficiently high thermal strain during the training sessions (Sotiridis, Ciuha, *et al.*,

2020; Sotiridis, Debevec, *et al.*, 2020). As a result, the ergogenic effect of hypoxic acclimation on maximal oxygen uptake measured in the heat might not be attributed to a training effect (Sotiridis, Debevec, McDonnell, *et al.*, 2018).

Dehydration is often sought to be avoided during exercise in the heat however this is not always accomplished. In addition, there could be potential physiological mechanisms whereby dehydration acts as an independent stressor to stimulate some heat acclimation responses, such as the expansion in plasma volume (Garrett *et al.*, 2014). Research investigating combined medium-term isothermal heat acclimation has examined whether moderate hypohydration will augment the acquisition and magnitude of heat adaptation responses (Neal *et al.*, 2015, 2016; Costello *et al.*, 2018).

The ergogenic effects of environmental stressors are often investigated in an attempt to improve endurance exercise performance. More attention has been given to heat acclimation in recent years as an accelerated alternative to the potential ergogenic effects of hypoxia for performance in cooler normoxic environments (Minson and Cotter, 2015; Nybo and Lundby, 2015) and this could occur through thermal and non-thermal physiological mechanisms (Corbett *et al.*, 2014). Research supports both evidence for an ergogenic effect (Shvartz *et al.*, 1977; Sawka *et al.*, 1985; Scoon *et al.*, 2007; Lorenzo *et al.*, 2010; Buchheit *et al.*, 2011, 2013; McCleave *et al.*, 2017) and for no effect (Karlsen *et al.*, 2015; Keiser *et al.*, 2015; Mikkelsen *et al.*, 2019) (Karlsen et al., 2015; Keiser et al., 2015; Mikkelsen et al., 2019) however these differences are likely due to methodological considerations and individual heat acclimation responses (Corbett *et al.*, 2018).

Questions

1. Discuss the evidence and mechanisms for heat acclimation to enhance physiological responses across a spectrum of exercise intensities, and maximal exercise performance, in hypoxia.
2. Your athlete aims to participate in the classic marathon scheduled for November 2020 in Athens. Due to the possibility of a second wave of COVID-19 infections, the organizers are thinking of moving the event earlier i.e. late September (with the ambient temperature ranging between 18 and 28 °C in the morning hours), keeping it as initially scheduled or cancelling the event. The decision will not be taken until mid-September. What acclimation protocol (if any) would you incorporate into your athlete's training schedule to prepare them in the best possible way for the event?
3. Summarise the findings of literature surrounding combined heat acclimation with dehydration and describe the physiological mechanisms behind these.
4. Discuss the state of the literature on the ergogenic potential of heat and what remains to be uncovered to fully answer this question, in the context of exercise performance.

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