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## Interactions in human performance: An individual and combined stressors approach

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## Interactions in human performance: An individual and combined stressors approach\*

Comment on: Lloyd A, Raccuglia M, Hodder S, and Havenith G. Interaction between environmental temperature and hypoxia on central and peripheral fatigue during high-intensity dynamic knee extension. *J Appl Physiol* 2016; 120: 567–79; <http://dx.doi.org/10.1152/jappphysiol.00876.2015>

### Environmental extremes: A multifactorial phenomenon

In many clinical, ergonomic and sporting contexts, humans are exposed to environments that are suboptimal for physical and cognitive performance. This has prompted a substantial body research on the human response to heat, cold, hypoxia, noise, vibration, hypo- and hyperbaria, as well as hyper- and microgravity. However, working at environmental extremes can expose individuals to more than just a single stressor. Indeed, it is the combination of stressful factors which characterizes the ‘extreme’ nature of environments like high-altitude (e.g. hypobaric hypoxia, cold, solar radiation), deep-sea (e.g., hyperbaria, cold, inspiratory gas toxicity) and space (e.g. heat, cold, hypobaric normoxia, hyper- and microgravity).

### Are combined stressors really that common?

Combined stress is not just typical of extreme environments. In fact, advances in technology have created a number of novel working and recreational environments which represent a challenging and complex arrangement of psychological and physiological stressors. For example: driverless cars, virtual reality simulation and space tourism each integrate classical stressors such as whole-body vibration, visual strain and solar radiation, with more unusual stressors such as weightlessness, powerlessness (a sense of loss of control) and visio-vestibular conflict.

### Are multifactorial environments just too complex to quantify?

Despite a high prevalence of multifactorial environments, scientific understanding of how combined stressors can influence humans’ physical and cognitive capacities remains extremely limited. An explanation for the dearth of interaction specific studies is that such approaches can be experimentally, temporally and practically challenging.<sup>1</sup> Moreover, the results are often difficult to interpret. That stated, this can - to some extent - be lessened by a clearer understanding of the characteristics of interactions as well as their role in the operation of dynamic systems.

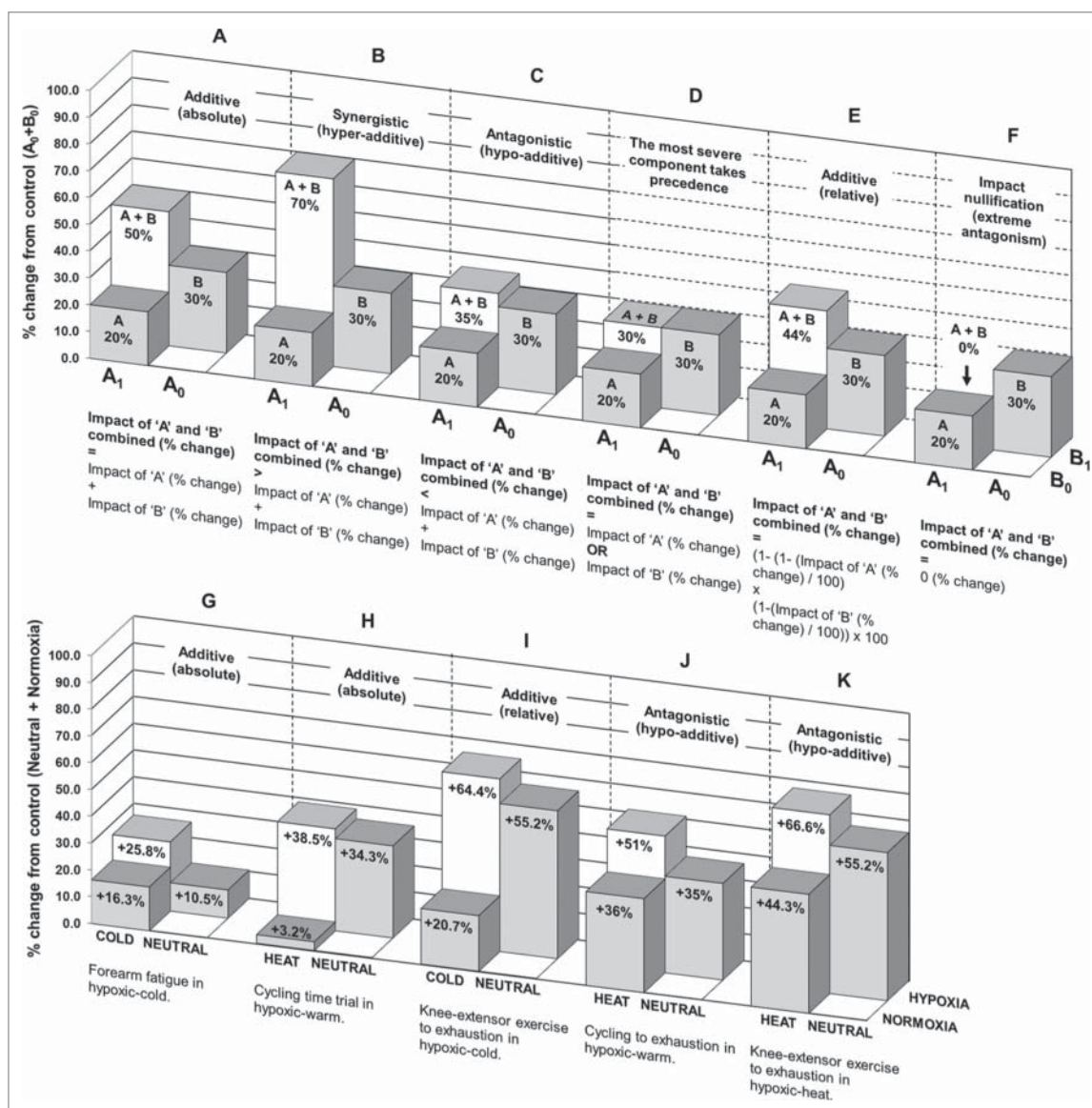
### Understanding and characterizing interactions

The combined effect of 2 or more stressors can be categorised by their net effect; typically under 3 classifications. The first type is an effect that is additive (summative; Fig. 1A). When using ANOVA, additive is the statistical ‘null hypotheses’ of interactions i.e. no differential effect of either stressor in the presence of the other stressor. The second possibility is a net effect that is significantly more than the additive effect. This is termed a synergistic or hyper-additive interaction (Fig. 1B). Finally, it is possible to have a net effect that is significantly less than the additive effect. These are antagonistic, subtractive or hypo-additive interactions (Fig. 1C).

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**Figure 1.** Interactions in human physiology and performance. (A, B and C) show the 3 types of interaction (additive, synergistic, antagonistic) that can occur when combining independent stressors. (D, E and F) show examples of 3 interaction sub-types ('the most severe component takes precedence', 'relative addition' and 'impact nullification'). (G to K) shows the recent studies (refs. 3, 5, 4, 2 and 4 respectively) that have employed an individual and combined stressors approach to investigate human performance under thermal and hypoxic stress. Together these studies provide evidence that as the individual stressors impact increases, there is a progressive shift from additive to antagonistic (hypo-additive) interactions.

### Sub-sets of additive, antagonistic and synergistic interactions

Within these interaction types, some sub-classifications are possible, including the 'most severe component' (i.e., the impact of one stressor cancels out the other; Fig. 1D) and 'relative addition' (Fig. 1E). Relative addition is a sub-set of both additive and antagonistic interactions; it occurs when the impact percentage - rather than the absolute value - remains the same in the presence of another stressor. This may have most relevance when time is the outcome variable. Extreme antagonistic interactions can also result in 'impact nullification' (Fig. 1D); whereby the combined effect is lower than the individual effects, right up to the point where the total impact disappears.

## General principles affecting interactions

Since it is not possible to quantify all the stressor interactions known to occur in nature, it is important to elucidate the overarching mechanisms influencing interaction expression. In this regard, Broadbent,<sup>1</sup> and Lloyd et al.<sup>3</sup> each proposed - from within their respective fields - that interactions between stressors may be linked to their physiological and/ or psychological 'mechanisms of action'. They suggested that additive effects may result from combining stressors with independent mechanisms; while interactive effects could arise when combining stressors that are mechanistically similar. This idea operates on the basis that for one stressor to influence the expression of another, the 2 factors must share a common pathway of action.

## Hypoxia and thermal stress as a model for understanding interactions

The two most prominent stressors at altitude are cold ambient temperatures and low levels of oxygen (hypoxia). Currently, only 2 studies have examined the individual and combined effects of cold and hypoxia (hypoxic-cold) on performance at altitude<sup>3,4</sup> (Fig. 1G and 1I). For comparative purposes, Lloyd et al.<sup>4</sup> also examined a combination of severe heat stress and hypoxia (hypoxic-heat) (Fig. 1K). As well as these, 2 other studies have employed an individual and combined stressors approach to examine hypoxic-heat during exhaustive cycling<sup>2,5</sup> (Fig. 1H and 1J).

## Interaction type and the individual stressors' impact

By observing the individual and combined impacts across the studies presented in Fig. 1 (Panels G–K) Lloyd et al.<sup>4</sup> proposed a novel principle explaining the interaction between multiple stressors on human performance. Rather than the mechanism of action (see above), this principle suggests that the impact magnitude of the individual stressors' effect on exercise capacity is what dictates the type of interaction expressed between stressors. Mild stressors produce additive effects; however as the individual stressors' impact increases (moving rightward in Figure 1G–1K) there is a progressive shift from additive to antagonistic interactions. This infers a maximum threshold for performance deterioration, whereby humans respond to very severe and simultaneous strains based on the 'most severe strain takes precedence' principle.

## What could this mean for integrative exercise science?

Characterizing interactions between 2 or more system inputs provides a useful model for understanding multi-strain integration and its impact on human physiology and performance. On this basis, it may be that a progressive hypo-additive principle could also underpin other biological phenomena which are known to be influenced by numerous psycho-physiological pathways, such as the control of breathing, autonomic thermoregulatory responses to regional body temperatures, behavioral thermoregulation, as well as the decision to regulate or stop exercise. In particular, this more flexible paradigm could elucidate why the predominant limiting factors affecting human performance are often dynamic, varied and task specific.

## Additional considerations

Currently, hypo-additive responses have only been reported in temporal variables e.g., time to exhaustion (Fig. 1I–1K). Thus, it is possible that a 'time squeezing' effect can explain the progressive shift from additive to antagonistic (hypo-additive) interactions. Moreover, while additive and antagonistic interactions are implicated in this model, synergistic (hyper-additive) responses are known to occur in many physiological contexts e.g. when two stressors, such as cold and rain, both result in the same physiological strain i.e. body cooling. How this integrates with a progressive hypo-additive paradigm is not yet clear. As such, substantial experimental work remains necessary to validate the paradigm proposed by Lloyd et al.<sup>4</sup> In any case, the present findings do demonstrate the value of adopting an individual and combined stressors approach. That is to say, in order to appreciate a multi-factorial phenomenon, you must consider a multi-factorial approach.


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