Eur J Appl Physiol (2009) 106:317–319
DOI 10.1007/s00421-009-1039-0

REPLY

Authors' response to H. Daanen's 'cold-induced vasodilation' letter

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Accepted: 10 March 2009 / Published online: 21 March 2009

We appreciate the letter of Dr. Daanen (Daanen 2009) with regards to our methodology for inducing cold-induced vasodilation (CIVD) in our experiment (Flouris et al. 2008) as it creates a much-needed opportunity to discuss this vital aspect of CIVD that has not received much attention. It has been observed for some time now that a wide variety of CIVD-inducing techniques have been adopted (Sendowski et al. 1997). Water immersion has been used in many experiments, yet the water temperature varies between 0°C (Adams and Smith 1962; Daanen and van der Struijs 2005) and 8°C (Daanen et al. 1997; Reynolds et al. 2007) while the immersion time varies between 1 and 40 min (Sendowski et al. 1997; Daanen and Ducharme 1999). CIVDs have been also recorded during conductive cooling from touching cold materials (Havenith et al. 1992; Chen et al. 1994), while many experiments have adopted local or whole body exposures to cold air. With regards to local air exposure, air temperatures ranging from 10 to −18°C have been used to cool the fingers for 2 h in order to induce CIVD (Kramer and Schulze 1948). On the other hand, whole body exposures of 10°C (Montgomery and Williams 1977; Brajkovic and Ducharme 2006), 1°C (Steegmann Jr 1979), 0°C (Shitzer et al. 1998a; Brajkovic and Ducharme 2006), −7°C (Santee et al. 1990), −10°C (Brajkovic and Ducharme 2006), and −17°C (Shitzer et al. 1991, 1998b; Shitzer 1998) lasting up to 2 h have been adopted as CIVD-inducing techniques in humans. Experiments in rats have identified CIVDs in whole body exposures at ambient temperatures of 5 and 10°C (Berry et al. 1984). Our experiment (Flouris et al. 2008) incorporated a 130-min exposure to −20°C, a protocol that creates the most severe cold stress of all whole body air exposure experiments in the CIVD literature to date.

During the cold exposure in our experiment, participants wore commercially available clothing simulating all three layers of the Improved Environmental Clothing System Canadian Forces Arctic clothing ensemble (3.6 clo, 0.556 m^2 K W^{-1}), while the hands were insulated with thin gloves and Arctic mitts (1.2 clo, 0.185 m^2 K W^{-1}). Dr. Daanen argues that '…the extremities were not exposed to cold and the term CIVD thus seems inappropriate'. Furthermore, he argues that mean body temperature in our experiment was relatively high which suggests that '…it is more likely that the observed temperature fluctuations are attempts of the body to release body heat as a part of the normal thermoregulatory process; rather than an expression of CIVD' (Daanen 2009). While this scepticism appears logical, it is important to note that equivalent insulation of the body and hands has been used in several studies in the past (Santee et al. 1990; Shitzer et al. 1991, 1998a, b; Shitzer 1998), all of which incorporated shorter and less severe exposures compared to ours but reported a large number of CIVDs. Furthermore, finger temperature in our experiment was often as low as 5°C, confirming that the cold stimulus to the hands was strong enough to evoke CIVD.

Our hypothesis of a causal link between body temperature and CIVD is supported in several investigations (Takano and Kotani 1989; Daanen et al. 1997; Daanen and Ducharme 1999; Daanen 2003) that reported increased CIVD prevalence rates at higher levels of body temperature. In addition, it is generally agreed that there is a central component in CIVD given that normothermic and/or

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centrally warm humans demonstrate accelerated CIVD responses (Takano and Kotani 1989; Daanen et al. 1997), while those that are centrally cold reveal CIVDs of delayed onset and lesser magnitude (Keatinge 1957; Elsner et al. 1960; Werner 1977; Daanen et al. 1997). However, previous investigations did not arrive to our conclusions, probably because they did not assess the link between CIVD and body temperature in real-time but only through repeated-measures designs incorporating conditions of hyper-, hypo-, and normo-thermia. By establishing the link between body heat content and CIVD in real time minute-by-minute data, the CIVD phenomenon becomes systematic and interpretable in terms of biological control processes.

It is important to note that we also were sceptical of our initial results and, soon after our first experiment, we conducted a subsequent investigation (Flouris and Cheung 2009) to confirm our findings. In a recently published study we examined the effect of thermal balance perturbation on CIVD through a dynamic A-B-A-B design applying heat (condition A) and cold (condition B) to the body's core while the hand is exposed to a stable cold stimulus. Applications of heat and cold were achieved through water immersions in two tanks maintained at 42 and 12°C water temperature, respectively, in an A-B-A-B fashion. Throughout the experiment, the participants' right hand up to the ulnar styloid process was placed inside a temperature-controlled box set at 0°C air temperature. Our results demonstrated that CIVD occurred only during condition B and at times when body heat content was decreasing but rectal temperature had not yet dropped to baseline levels. Following the occurrence of all CIVDs, rectal temperature was reduced and the phenomenon ceased when rectal temperature fell below baseline. Heart rate variability data obtained prior to and during CIVD demonstrated a shift of autonomic interaction towards parasympathetic dominance which was due to a sympathetic withdrawal. Receiver operating characteristics curve analyses demonstrated that the CIVD onset cut-off points for rectal temperature change and finger temperature were 0.62 and 16.76°C, respectively.

In conclusion, while our initial experiment adopted a less popular CIVD-inducing methodology, it is supported by many studies in the literature as well as by our subsequent work which provides clear evidence that CIVD is a centrally originating phenomenon caused by sympathetic vasoconstrictor withdrawal; it is dependent on excess heat, and it may be triggered by excess heat with the purpose of preserving thermal balance.

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