# **Cold-induced Vasodilation: A Meta-analysis**

H.A.M Daanen<sup>1\*</sup>, R. S. Weller<sup>2,3</sup>, J. Buczny<sup>1</sup>

<sup>1</sup>Vrije Universiteit Amsterdam, The Netherlands <sup>2</sup>Naval Health Research Center, San Diego, California, USA <sup>3</sup>Leidos, Inc., San Diego, California, USA \*Correspondence: <u>h.a.m.daanen@vu.nl</u>

Keywords: Finger, Cold, Immersion

### Introduction

It is almost a century ago that Sir Thomas Lewis first described the phenomenon of cyclic changes in finger skin temperature when the finger is immersed in cold water [1], a reaction called cold-induced vasodilation (CIVD). Since then, several hundred studies have been performed to further elucidate the underlying mechanisms and the effects of interventions such as residence in cold and/or altitude or certain pharmaceutical agents. It is the purpose of this meta-analysis to provide an overview of CIVD responses from subjects worldwide prior to the interventions. Thus, we aim to provide insight in how the CIVD parameters are interrelated and dependent on ambient factors, such as water and ambient temperature and personal factors like age, sex, and ethnicity.

### Methods

The following databases were utilized in the meta-analysis: 1) Scopus derived database with keywords "cold induced vasodilation" OR "cold-induced vasodilation" OR "cold induced vasodilation" and 2) A database of 45 articles collected by the first author over the years regarding CIVD. Studies including pathology or children were excluded. Only finger/hand immersions of 30 minutes or more and in water lower than 20°C were included. The dependent variables were onset time, minimum finger skin temperature (Tmin) at onset time, maximum finger skin temperature of the first CIVD wave (Tmax) and mean finger skin temperature during immersion (Tmean). Amplitude was defined as Tmax – Tmin. Interdependence was determined using correlation analysis. A Forest plot was made to show variability for onset time.

# **Results and Discussion**

# Description of included studies

Out of 225 screened studies, 80 remained for further analysis. The database of 80 studies contained 130 populations that were evaluated. Only in 9 studies comparisons were made within subjects; most studies compared groups of people. In total, 358 females (16%) and 1,823 males (84%) were included. The dominating countries in the population dataset were Japan (31), Canada (18), India (18), Slovenia (17), USA (15) and Korea (10). Only one study had a group of 10 participants from African descent [2]. In 53% of the datasets, the hands were immersed to the wrist level; in 40% of the datasets only the middle finger was immersed and in 5% the index finger only. Prewarming was performed in 29% of the datasets. Immersion water temperature was approximately 4°C in 30% of the datasets, 26% in ice water, 22% at 8°C, 14% at 5°C and only 3% at 10°C. The age was under 20 years in 15%, from 20-30 years in 64%, from 30-40 years in 15% and over 40 years in 7% of the datasets. To reflect the general level of the differences, we calculated P. Using a bootstrap resampling procedure, we found that the total level of heterogeneity was 98.50, 95% CI [97.91, 98.87], whereas  $P_{\text{between}} = 69.55$ , 95% CI [0.00, 93.42] and  $P_{\text{within}} = 28.91$ , 95% CI [5.13, 98.24], suggesting that the distribution of the true mean values was more diverse between studies than within studies.

# Interrelation between dependent variables

All dependent variables were available in 56 datasets. Tmax was highly correlated to Tmean (0.83) and Tmin (0.78). Tmax and Tmin were interrelated (0.71). Amplitude was significantly related to Tmin (-0.40), Tmax (0.30) and onset time (-0.27).

#### Symposium 4

First Author and Publication		Mean [95% Cl]
O'Brien, 2003b	, <b> +</b>   ,	4.15 [ 3.86, 4.44]
Lee, 2017		4.20 [ 2.34, 6.06] 4.20 [ 3.49, 4.91]
Ko, 2020		4.30 [ 3.49, 5.11]
Lee, 2013		4.40 [ 3.34, 5.46]
Lee, 2017 O'Brien, 2005		4.40 [ 4.05, 4.75] 4.47 [ 4.10, 4.84]
O'Brien, 2005		4.52 [4.11, 4.93]
Kim, 2018		4.60 [ 4.20, 5.00] 4.74 [ 4.29, 5.19]
Lee, 2017		4.80 [4.21, 5.39]
O'Brien, 2015	, <del> - </del> ,	5.10 [ 4.71, 5.49]
So, 1975 VanderStruijs, 2008		5.10 [ 3.53, 6.67] 5.10 [ 4.04, 6.16]
Alba, 2023 O'Brian, 2003a	` <b> =</b> ]'	5.28 [ 4.69, 5.87]
Felicijan, 2008		5.60 [ 3.53, 7.67]
Sera, 2020 Sendowski, 2000		5.60 [ 5.32, 5.88] 5.62 [ 4.97, 6.27]
Ko, 2020		5.70 [ 3.96, 7.44]
Suganara, 1988 Sendowski, 1997	[ <b>≠</b> ]	5.90 [ 5.27, 6.53]
Tyler, 2015 Sugawara, 1997		5.90 [ 4.97, 6.83] 5.94 [ 5.12, 6.76]
Sugahara, 1996		6.00 [ 5.15, 6.85]
Hurlich, 1979		6.20 [ 1.71, 10.69]
Milliner, 2020		6.40 [ 5.10, 7.70]
Sugahara, 1996		6.50 [ 5.33, 7.67]
Park, 2016 Daanen, 2005	<b>4</b>	6.55 [ 6.38, 6.72] 6.70 [ 6.24, 7.16]
Mathew, 1979b	┝╼┤	6.70 [ 6.03, 7.37]
Sugawara, 1988 Sugawara, 2004		6.90 [ 5.68, 8.12]
Kume, 2006 Mathew, 1979a		7.00 [ 6.52, 7.48]
Sugahara, 1993	- <mark></mark> -	7.03 [ 6.26, 7.80]
Okamoto, 1995 Sugawara, 1997		7.14 [ 7.02, 7.26] 7.14 [ 6.44, 7.84]
Hoffman, 1990		7.15 [ 5.81, 8.49]
Tanaka, 1986	. [++].	7.18 [ 6.61, 7.75]
Daanen, 1999 Sugahara, 1996		7.20 [ 5.68, 8.72] 7.38 [ 6.65, 8.11]
Hurlich, 1979		7.40 [ 4.09, 10.71]
Mathew, 1979b		7.50 [ 6.52, 8.48]
Sugahara, 1983 Sauvet, 2012		7.56 [ 6.92, 8.20] 7.58 [ 6.76, 8.40]
Lee, 2021	[+ <b>=</b> -]	7.60 [ 7.04, 8.16]
Sugawara, 1993 Sugawara, 2004		7.76 [ 6.81, 8.71]
Mathew, 1979a Sugahara, 1982		7.80 [ 6.37, 9.23] 7.81 [ 7.43, 8.19]
Sugawara, 2004	<u>F</u> ∙4	7.96 [ 7.25, 8.67]
Mathew, 1979a		8.10 [ 6.71, 9.49]
Purkayastha, 1992 Sellers, 2023		8.20 [ 7.61, 8.79] 8.20 [ 5.86, 10.54]
Konda, 1981	, ' H=1 ' ,	8.25 [ 7.80, 8.70]
Hoffman, 1990		8.33 [ 4.41, 12.25]
Sugahara, 1982 Sugahara, 1983		8.36 [ 7.40, 9.32] 8.43 [ 7.53, 9.33]
Livingstone, 1976	, "H",	8.50 [ 8.24, 8.76]
Lee, 2013		8.60 [ 4.74, 12.46]
Wakabayashi, 2023 Geurts, 2005b		8.68 [ 8.11, 9.25] 8.90 [ 5.65, 12.14]
Lee, 2021	',⊢∙ , '	8.90 [ 7.64, 10.16]
Park, 2016		8.94 [ 8.39, 9.49]
Livingstone, 1976 Tyler, 2015		9.00 [ 8.78, 9.22] 9.00 [ 8.05, 9.95]
Sugahara, 1982	, <b>\-</b> -/ ,	9.02 [ 8.14, 9.90]
Sendowski, 1997		9.37 [ 7.21, 11.53]
Bridgman, 1991 Livingstone, 1976		9.38 [ 6.49, 12.27] 9.40 [ 9.09, 9.71]
Maley, 2014		9.56 [ 6.56, 12.56]
So, 1975		9.90 [ 6.20, 13.60]
Tsoutsoubi, 2022		9.95 [ 8.74, 11.16]
Livingstone, 1976		10.10 [ 9.83, 10.37]
Purkayastha, 1992 Purkayastha, 1992		10.20 [ 7.85, 12.55] 10.50 [ 6.19, 14.81]
Purkayastha, 1993		10.50 [ 6.19, 14.81]
Daanen, 1997		10.60 [ 6.68, 14.52]
Ciuha, 2021 Mathew, 1979a		11.00 [ 9.14, 12.86] 11.00 [ 9.57, 12.43]
Norrbrand, 2017	, <b>h</b> • • • • •	11.06 [ 9.65, 12.47]
Daanen, 2012		11.30 [ 7.53, 15.07]
Maley, 2014 Purkayastha. 1993		11.35 [ 6.60, 16.10] 11.50 [ 7.97, 15.03]
Wickham, 2021	· ⊢•-1	12.31 [11.32, 13.30]
Kingma, 2019		12.47 [ 9.53, 15.41] 12.70 [10.95, 14.45]
Sendowski, 2000 Geurts, 2006a		12.81 [ 6.99, 18.63] 13.50 [ 7.68, 19.32]
Sellers, 2023 Maley, 2014		14.30 [11.75, 16.85]
Geurts, 2005a		17.30 [15.43, 19.17]
RE Model		7.86 [ 7.39, 8.33]
		evenere transition (2000)
0	0 2.0 5.0 10.0 15.0 20.0 22.5	

Effect Size (Mean)

# Forest plot

The forest plot for onset time is shown on the left, indicating large variability within and between datasets. The slowest onset times were found in people with African descent [2], and in studies where electrical stimulation was applied during immersion.

#### Conclusions

We conclude that CIVD methodology is not standardized and has primarily focused on young white male populations. CIVD parameters are highly variable within and between studies, partly due to differences in methodology. CIVD parameters are interrelated, suggesting that one or two cluster terms may be indicative of the magnitude of the CIVD response.

#### References

Lewis T (1930) 1. Observations upon the reactions of the vessels of the human skin to cold. Heart 15, 177-208. 2. Maley MJ, Eglin CM, House JR, Tipton MJ (2014) The effect of ethnicity on the vascular responses to cold exposure of the extremities. European Journal of Applied *Physiology* 114 (11), 2369-2379. doi:10.1007/s00421-014-2962-2.