## Temporal Contrast Enhancement in Thermosensation: A Framework for Understanding Paradoxical Heat Sensation

Alexandra G. Mitchell<sup>1</sup>\*, Jesper Fischer Ehmsen<sup>1</sup>, Małgorzata Basińska<sup>2</sup>, Arthur S. Courtin<sup>1</sup>, Rebecca A. Böhme<sup>1,3</sup>, Camila Sardeto Deolindo<sup>1</sup>, Micah G. Allen<sup>1,4</sup>, Kristian Sandberg<sup>1</sup>, & Francesca Fardo<sup>1,5</sup>\*

## **Supplementary Materials**



*Supplementary Figure 1*: Innocuous and noxious TSL threshold values for each contrast condition (starting temperature) for veridical experience of cold and PHS.



**Supplementary Figure 2**: Density plots of the distribution of (A) innocuous and (B) noxious TCF and changes in distribution by calculating the log10 of (C) innocuous and (D) noxious TCF, which was used in the final logistic regression. As the TCF is a standardised threshold value, the distribution of innocuous and noxious TSL thresholds match that of the raw TCF, just over a different scale.

**Supplementary Tables 1-12:** Full results for fixed effects in all models presented in the manuscript with associated omnibus tests

### Model 1A: PHS ~ contrastCondition \* task + (1|ID)

1A Regression Parameters						
	β	SE	z-value	<i>p</i> -value	OR [95% CI]	
Intercept	-4.29	.29	-14.86	<.001	.01 [.0102]	
32 vs. 38°C	.57	.29	1.97	.05	1.77 [1.00 – 3.14]	
32 vs. 44°C	1.62	.26	6.12	<.001	5.05 [3.00 - 3.14]	
Innoc. vs nox.	.90	.28	3.23	.001	2.46 [1.43 – 4.27]	
38°C * nox.	94	.38	-2.45	.01	.39 [.1983]	
44°C * nox.	-2.38	.38	-6.26	<.001	.09 [.0420]	

Supplementary Table 1

# Supplementary Table 2

1A Omnibus Test						
$\chi^2$ df <i>p</i> -value						
contrastCondition	12.52	2	.002			
task	3.24	1	.07			
contrastCondition*task	40.47	2	<.001			

### Model 2A: innocuousTSL ~ contrastCondition + trial\_z + (1|ID)

Supplementary Table 3	
-----------------------	--

2A Regression Parameters						
	β	SE	df	t-value	<i>p</i> -value	
Intercept	29.85	.10	438.12	307.28	<.001	
32 vs. 38°C	46	.10	1661.00	-4.86	<.001	
32 vs. 44°C	95	.10	1661.00	-9.95	<.001	
Trial	16	.04	1661.28	-4.19	<.001	

Supplementary Table 4

2A Omnibus Test						
	$\chi^2$	df	<i>p</i> -value			
contrastCondition	98.94	2	<.001			
trial_z	17.58	1	<.001			

### Model 2B: noxiousTSL ~ contrastCondition + trial\_z + (1|ID)

supplementary ruble 5						
2B Regression Parameters						
	β	SE	df	t-value	<i>p</i> -value	
Intercept	11.72	.64	221.76	18.26	<.001	
32 vs. 38°C	1.86	.20	1661.00	9.05	<.001	
32 vs. 44°C	2.12	.20	1661.00	10.36	<.001	
Trial	92	.08	1661.05	-11.04	<.001	

Supplementary Table 5

### Supplementary Table 6

2B Omnibus Test						
	$\chi^2$	df	<i>p</i> -value			
contrastCondition	127.33	2	<.001			
trial_z	121.89	1	<.001			

# Model 2C: innocuousPHS ~ innocuousTSL \* noxiousTSL + (1|ID)

2C Regression Parameters							
	β	SE	z-value	<i>p</i> -value	OR [95% CI]		
Intercept	-7.56	.70	-11.30	<.001	<.01 [<.01 - <.01]		
Innocuous TSL	-1.56	.11	-14.18	<.001	.21 [.17 – .26]		
Noxious TSL	.94	.22	4.37	<.001	2.56 [1.68 - 3.91]		
Innoc. * nox.	68	.10	-7.02	<.001	.51 [.42 – .61]		

Supplementary Table 7

### Model 3A: innocuousPHS ~ contrastCondition + (1|ID)

3A Regression Parameters					
	β	SE	z-value	<i>p</i> -value	OR [95% CI]
Intercept	-4.71	.39	-12.43	<.001	.01 [<.0102]
32 vs. 38°C	.61	.30	.207	.04	1.83 [1.02 – 3.29]
32 vs. 44°C	1.72	.28	6.19	<.001	5.58 [3.24 - 9.61]

Supplementary Table 8

### Supplementary Table 9

3A Omnibus Test					
	$\chi^2$	df	<i>p</i> -value		
contrastCondition	45.89	2	<.001		

# Model 3B: innocuousPHS ~ log(innocuousTCF) + (1|ID)

Supplementary Table 10	Suppl	lementary	Table	10
------------------------	-------	-----------	-------	----

3B Regression Parameters						
	β	SE	z-value	<i>p</i> -value	OR [95% CI]	
Intercept	-1.34	.38	-3.51	<.001	.26 [.1255]	
Innocuous TCF	1.37	.19	7.24	<.001	3.94 [2.72 - 5.70]	

# Model 3C: innocuousPHS ~ log(noxiousTCF) + (1|ID)

Supplementary T	Table	11
-----------------	-------	----

3C Regression Parameters						
β SE z-value <i>p</i> -value OR [95% CI]						
Intercept	-3.38	.32	-10.65	<.001	.03 [.0206]	
Noxious TCF	.38	.30	1.26	.21	1.46 [.81 – 2.65]	

Model 3D: innoc	uousPHS ~ log(inn	ocuousTCF) * lo	g(noxiousTCF	) + (	1 ID)
	<b> </b>		<b>A</b> (	<i>,</i> ,	

3D Rogrossion Parameters						
	β	SE	z-value	<i>p</i> -value	OR [95% CI]	
Intercept	91	.74	-1.23	.22	.40 [.09 – 1.72]	
Innocuous TCF	2.60	.49	5.35	<.001	13.48 [5.20 – 34.99]	
Noxious TCF	-1.22	.69	-1.77	.07	.29 [.08 – 1.14]	
Innoc. * Nox.	.46	.32	1.46	.15	1.58 [.85 – 2.94]	

Supplementary Table 12

**Supplementary Table 13**: Mean QST detection and pain thresholds (°C) for individuals without PHS compared to those with PHS. No significant relationship was observed between PHS prevalence and cold detection (CDT), warm detection (WDT), cold pain (CPT) and heat pain (HPT) thresholds.

	No PHS		PHS		
	Mean	SD	Mean	SD	
CDT	30.33	0.86	30.41	1.05	
WDT	33.86	0.61	33.98	0.86	
СРТ	14.23	9.11	17.80	9.44	
НРТ	42.81	3.43	42.17	3.65	

Supplementary Table 14: QST model results

innocuousPHS ~ $CDT + WDT + CPT + HPT + (1 ID)$					
	β	SE	z-value	<i>p</i> -value	OR [95% CI]
Intercept	-14.25	2.65	-5.38	<.001	<.01 [<.01 - <.01]
CDT	28	1.36	21	.84	.75 [.05 – 10.76]
WDT	.33	1.44	.23	.82	1.39 [.08 – 23.38]
СРТ	1.10	2.81	.39	.70	3.01 [.01 - 74.29]
НРТ	.83	2.71	.31	.76	2.27 [.01 - 46.48]

#### Supplementary Note 1: Trial number affects TSL thresholds but not PHS

We conducted an extension of Model 1A in the manuscript with the inclusion of trial number (z-scored) (Model S1). This was to account for the assumption that the probability PHS may be modulated by the trial number. We found no significant effect of trial on PHS (z = -0.67, p = .50, OR = 0.92, 95% CI = 0.71 – 1.18) and the addition of trial number did not significantly improve upon Model 1A (p = .91).

#### $PHS \sim contrastCondition * task + trial_z + (1|ID)$ (Model S1)

In addition to this, we included trial number (z-scored) into Models 2A and 2B. Both innocuous and noxious TSL temperatures decreased with increasing trial number (innocuous TSL:  $t_{438.12/1661.28} = -4.19$ ,  $\beta = -.16$ , p < .001; noxious TSL:  $t_{221.76/1661.05} = -11.04$ ,  $\beta = -.92$ , p < .001).

#### Supplementary Note 2: Effect of age and gender on TSL thresholds and PHS

We explored the possible effects of age and gender (male or female) on both TSL thresholds and PHS by adding these predictors to models 2A, 2B and 3D in the manuscript (Models S2,

S3 & S4). Neither age nor gender significantly affected innocuous (age:  $\beta = -.01$ , t = -.56, df = 213.10/205, p = .58; gender:  $\beta = -.15$ , t = -.90, df = 213.10/205, p = .37) or noxious (age:  $\beta$  = -.21, t = -1.74, df = 205.60/205, p = .08; gender:  $\beta$  = -1.15, t = -.89, df = 205.60/205, p = .37) TSL thresholds. PHS probability was also not significantly affected by age (z = -.63, p = .53, OR = .98, 95% CI = .91 - 1.05) or gender (z = 1.74, p = .08, OR = 1.93, 95% CI = .92 - 4.04).

 $\begin{array}{ll} innocuousTSL \sim contrastCondition + trial_z + age + gender + (1|ID). & (Model S2) \\ noxiousTSL \sim iontrastCondition + trial_z + age + gender + (1|ID) & (Model S3) \\ PHS \sim innocuousTCF * noxiousTCF + age + gender + (1|ID) & (Model S4) \\ \end{array}$