

Supplemental Materials

The effect of a neuronal nitric oxide synthase inhibitor on neurovascular regulation in humans

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Major Resources Table

Participant number	Age	Weight (kg)	Height (cm)	Sex	Ethnicity
001	36	63	165	F	Caucasian
002	26	70	178	M	Caucasian
004	24	65	160	F	Caucasian
007	42	70	167	F	South Asian
009	18	65	165	F	Caucasian
010	28	73	178	M	Caucasian
011	24	56	165	F	Caucasian
012	21	54	161	F	East Asian
013	25	53	160	F	East Asian
014	34	89	174	M	South Asian
015	26	64	173	M	Caucasian
016	25	82	180	M	East Asian
Mean (SD)	27.4 (6.7)	67.0 (10.8)	168.8 (7.4)	(7 F, 5M)	

Table S1 Participant characteristics

	Placebo control		SMTC		Pressor control	
	Pre	Post	Pre	Post	Pre	Post
MAP (%)	-0.23±0.4	0.15±0.5	0.17±0.6	-0.68±0.4	0.37±0.6	0.67±0.3
Mean PCAv (%)	8.1±0.6	8.8±0.5	7.6±1.0	6.7±1.0	6.82±0.6	8.10±0.7
Peak PCAv (%)	19.0±0.7	20.9±1.1	19.1±2.0	17.0±1.9	17.4±1.3	19.5±1.7
PCA PI (%)	-1.9±0.6	-2.2±0.5	-2.1±0.8	-2.5±0.9	-1.9±1.0	-3.1±0.6
PCA PR (%)	-3.5±0.5	-2.4±0.8	-3.0±0.5	-2.1±0.4	-3.1±0.6	-3.0±0.5
Time to peak (s)	18.8±2.4	16.2±2.4	19.1±1.9	15.5±2.6	15.4±2.1	14.1±2.2
Time to max slope (s)	5.7±0.7	7.3±1.7	5.5±0.5	6.1±0.5	5.3±0.2	4.9±0.1
Mean PCAv 0-5s (%)	5.5±0.8	7.2±0.5	5.6±0.9	4.5±0.9	4.7±0.8	7.3±0.8
Mean PCAv 5-10s (%)	13.1±0.9	15.2±0.9	13.1±1.8	12.2±1.6	12.7±1.2	16.2±1.4
Mean PCAv slope, 0-5s (%)	11.4±1.0	13.5±1.0	11.4±1.0	13.5±1.0	11.2±1.2	14.0±1.2
Max PCAv slope, 0-5s (%)	10.1±0.7	11.5±1.0	9.8±1.2	7.4±1.2	9.2±0.8	11.3±1.1
Minimum PCAv slope, 0-5s (%)	12.9±1.6	15.7±1.5	14.9±2.2	13.0±2.6	13.5±2.4	17.2±1.9

Table S2 NVC Results

PI, pulsatility index; PR, pulse ratio; PCAv, posterior cerebral artery velocity. Data expressed as mean±SEM

Subject	Placebo control	SMTC	Pressor control	Subject mean
1	7.59%	8.03%	7.51%	7.71%
2	9.69%	10.05%	9.15%	9.63%
4	6.66%	8.76%	6.95%	7.46%
7	5.54%	6.28%	8.03%	6.62%
9	8.34%	7.22%	5.40%	6.99%
10	10.25%	10.69%	9.74%	10.23%
11	5.25%	4.89%	6.72%	5.62%
12	6.37%	6.12%	5.59%	6.03%
13	8.13%	6.61%	8.27%	7.67%
14	6.07%	6.62%	6.22%	6.30%
16	9.79%	4.72%	5.36%	6.62%
Condition mean	7.61%	7.27%	7.18%	

Table S3 Coefficient of Variation Data

Variable	Placebo Control	SMTC	Pressor Control
Δ Average PCA velocity (cm/s)	W= 0.94 P= 0.53	W= 0.93 P= 0.40	W= 0.93 P= 0.38
Δ Average MCA velocity (cm/s)	W= 0.92 P= 0.34	W= 0.92 P= 0.35	W= 0.97 P= 0.85
Δ PCA CVR (mmHg/cm*s ⁻¹)	W= 0.91 P= 0.26	W= 0.82 P= 0.020	W= 0.96 P= 0.73
Δ MCA CVR (mmHg/cm*s ⁻¹)	W= 0.86 P= 0.060	W= 0.61 P= 3.1x10 ⁻⁵	W= 0.94 P= 0.50
Δ Average PCA velocity 0-5s (%)	W= 0.95 P= 0.70	W= 0.94 P= 0.57	W= 0.96 P= 0.73
Δ Average PCA velocity slope 0-5s (%)	W= 0.97 P= 0.86	W= 0.96 P= 0.77	W= 0.94 P= 0.49
Δ Time of max PCA slope	W= 0.90 P= 0.21	W= 0.83 P=0.031	W= 0.92 P= 0.38
Δ iRate 1	W= 0.98 P= 0.97	W= 0.96 P= 0.82	W= 0.94 P= 0.55
Δ iRate 2	W= 0.94 P= 0.51	W= 0.96 P= 0.81	W= 0.97 P= 0.85
Δ iAmp 1	W= 0.97 P= 0.90	W= 0.92 P= 0.30	W= 0.95 P= 0.61
Δ iAmp 2	W= 0.93 P= 0.36	W= 0.94 P= 0.48	W= 0.96 P= 0.73
Δ iPulse	W= 0.79 P= 0.0070	W= 0.84 P= 0.030	W= 0.97 P= 0.89
Δ PCA CVCi (cm/s/mmHg)	W= 0.84 P=0.031	W=0.85 P=0.037	W= 0.77 P= 0.0041
Δ PCA CVCi (%)	W= 0.95 P= 0.70	W= 0.93 P= 0.43	W= 0.91 P= 0.22
Δ NVC MAP (%)	W= 0.86 P= 0.064	W= 0.92 P= 0.32	W= 0.90 P= 0.16

Table S4 Shapiro-Wilk Normality Data

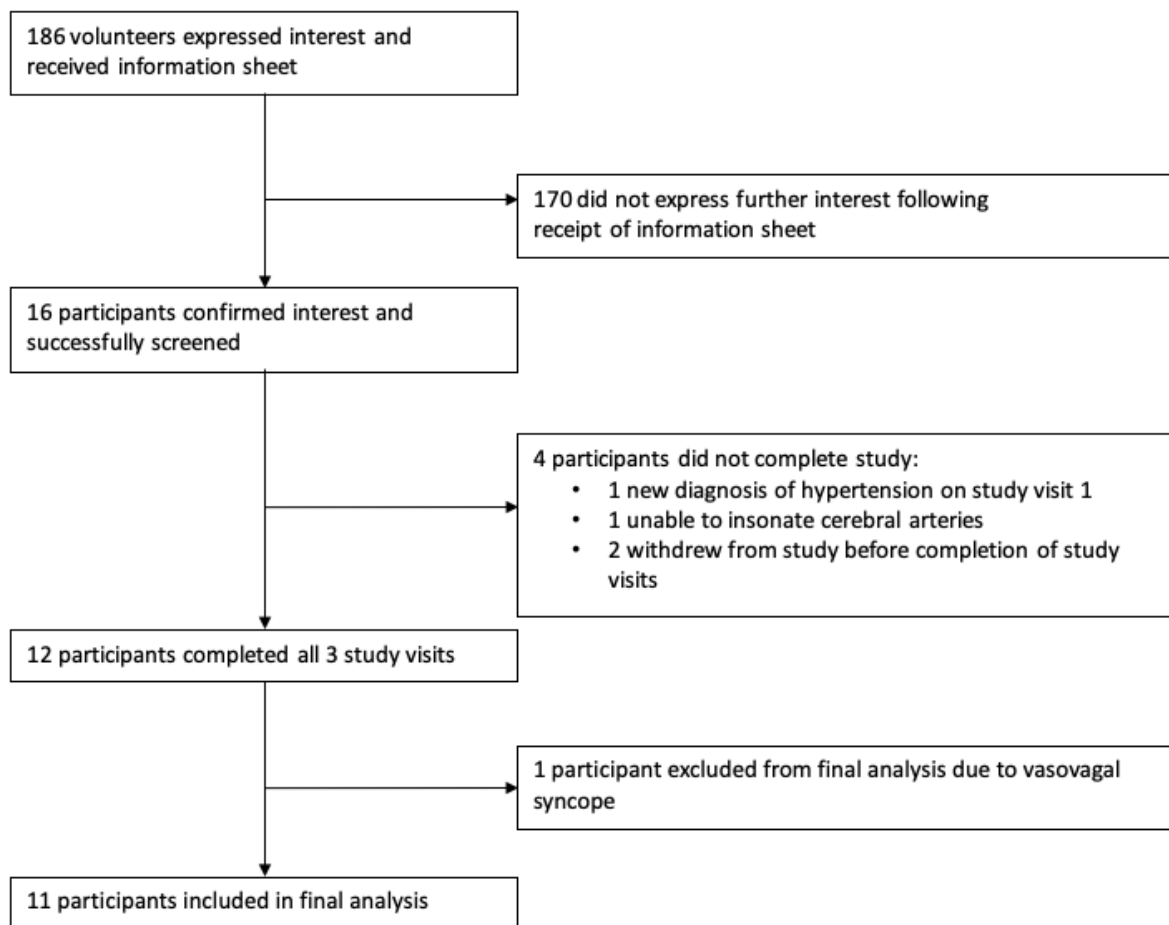


Figure S1. Study Participation

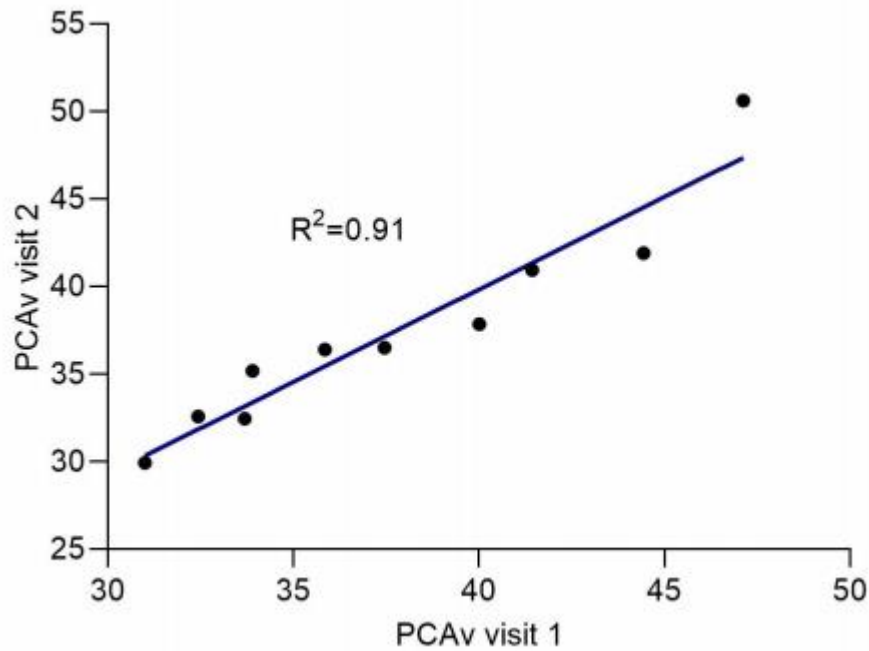


Figure S2. Test-retest reliability

Here we show our test-retest reliability for baseline PCA velocity values taken from 10 participants tested on 2 separate days, a minimum of 1 week apart. The evaluation of test-retest reliability using an intraclass correlation coefficient (ICC) is the preferred metric of use.⁴⁹ We report an ICC score of 0.951.

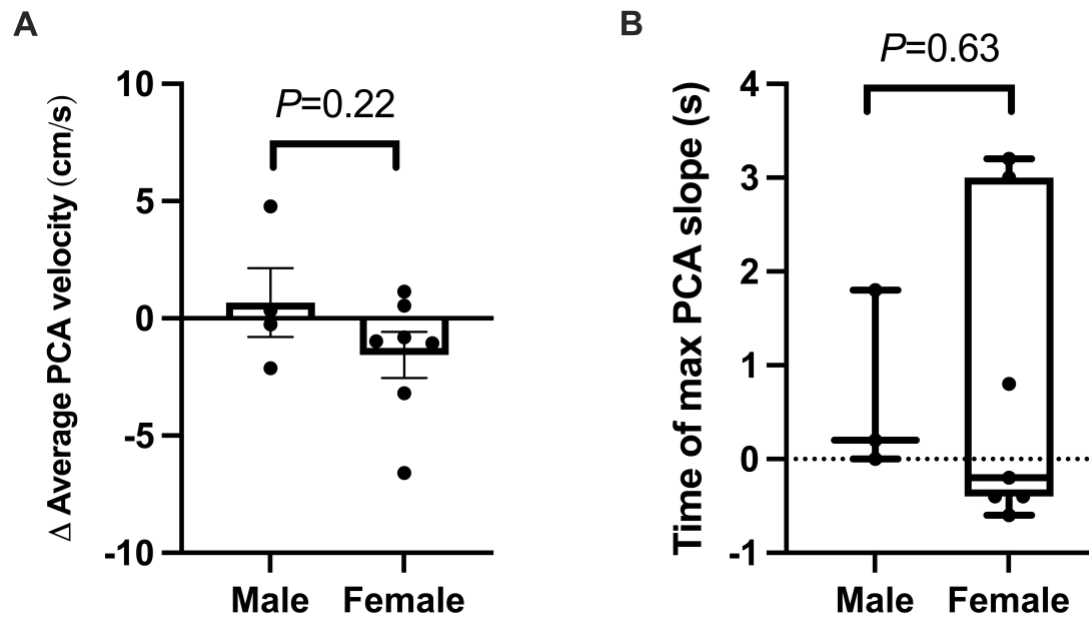


Figure S3. Analysis of sex-based differences in PCA responses to SMTC, as analysed by unpaired t test (panel A, mean \pm SEM) or Mann-Whitney test (panel B, median (IQR)). n=11 for panel A (4 male, 7 female), n=10 for panel B (3 male, 7 female).

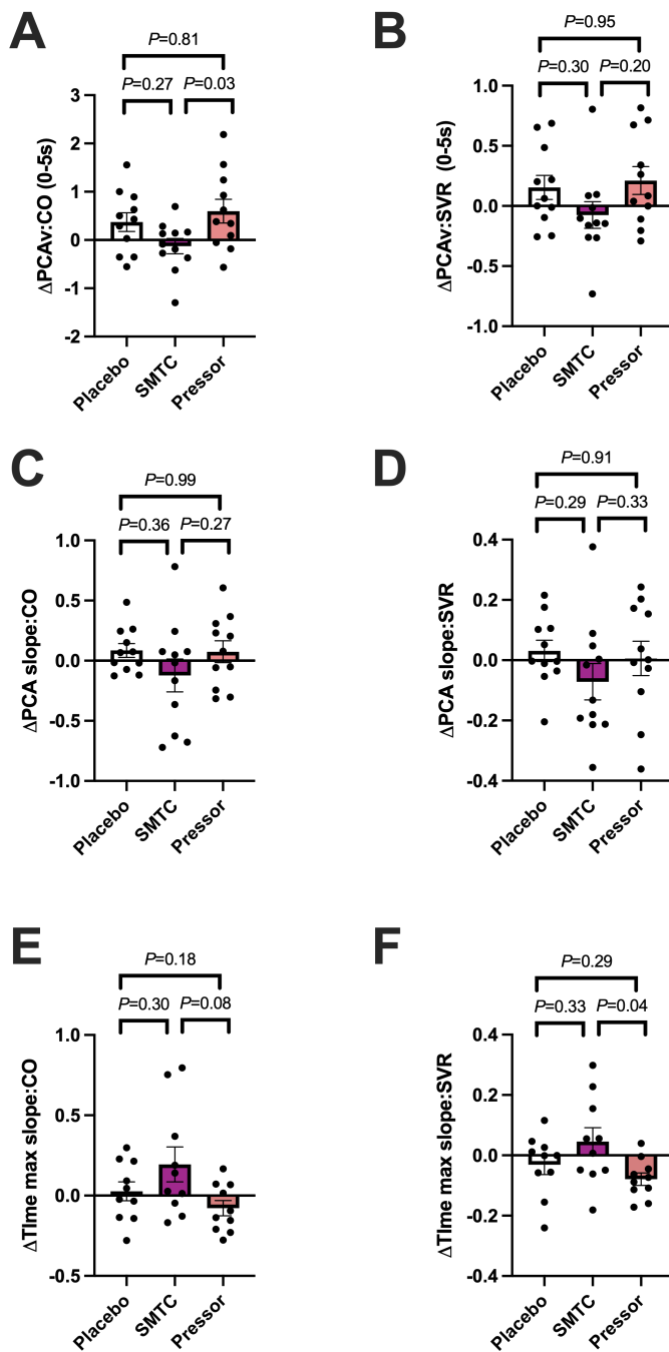


Figure S4. Changes in neurovascular coupling velocity corrected for changes in haemodynamic conditions. Panels A, C, E show indices corrected for CO. Panels B, D, F show indices corrected for SVR. Analysis performed using one way ANOVA and Tukey *post hoc*. Data presented as mean \pm SEM. n=11, apart from panels E&F (n=10).

Major Resources Table

Description	Source / Repository	Persistent ID / URL
Study drug: S-methyl-L-thiocitrulline	Merck Millipore, USA	
Study drug: Phenylephrine	Amdipharm UK Ltd	
Intellivue Brachial blood pressure monitor	Phillips, UK	
Finometer NOVA Finger plethysmograph	Finapres Medical Systems, The Netherlands	
Transcranial Doppler probes: DWL DopplerBox X	Compumedics, Singen, Germany	
QL Monitoring Software, version 3.5.5		
RespirAct	Thornhill Research, Toronto, Canada	
Tegaderm transparent dressing film	3M Healthcare, St Paul, Minnesota, USA	
iNVC Software, Version 2.2	Innovate Calgary, Alberta, Canada	