SUPPLEMENTARY FIGURES

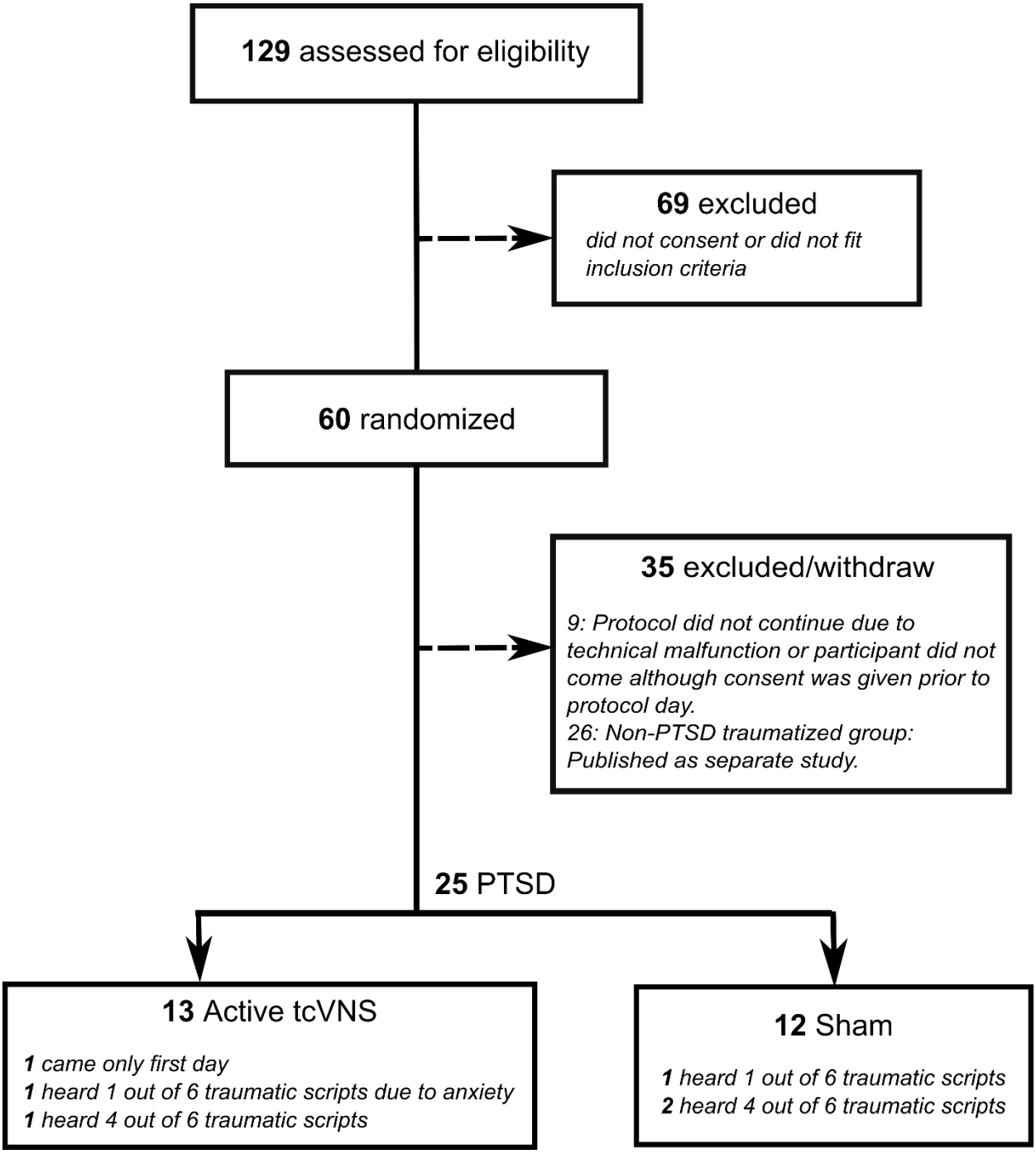


Figure S1. Consolidated Standards of Reporting Trials (CONSORT) diagram of the study.

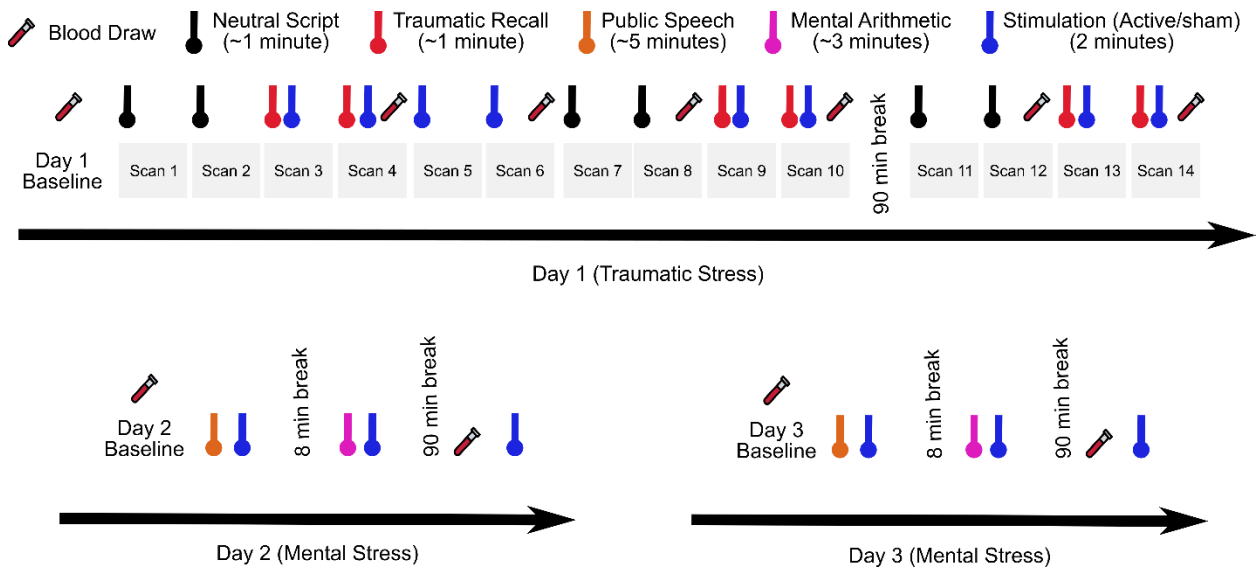


Figure S2. Protocol description. Three streams of data were collected: High resolution positron emission tomography (HR-PET) brain imaging (only first day), physiological signals (each day), and blood draws (each day). **(A)** The first day included 14 HR-PET scans (six neutral, six traumatic recall followed by stimulation, two stimulation without stress) where scripts were presented audibly through headphones while the subjects are laying down inside the scanner. After each traumatic stress prompt, stimulation (active or sham) was applied immediately. There was a 90-minute break after scan 10 on this day. **(B)** Second and third days included two types of mental stress, public speech and mental arithmetic. After each stressor, stimulation was applied immediately. After a 90-minute break from the mental stress protocol, participants received stimulation without acute stress.

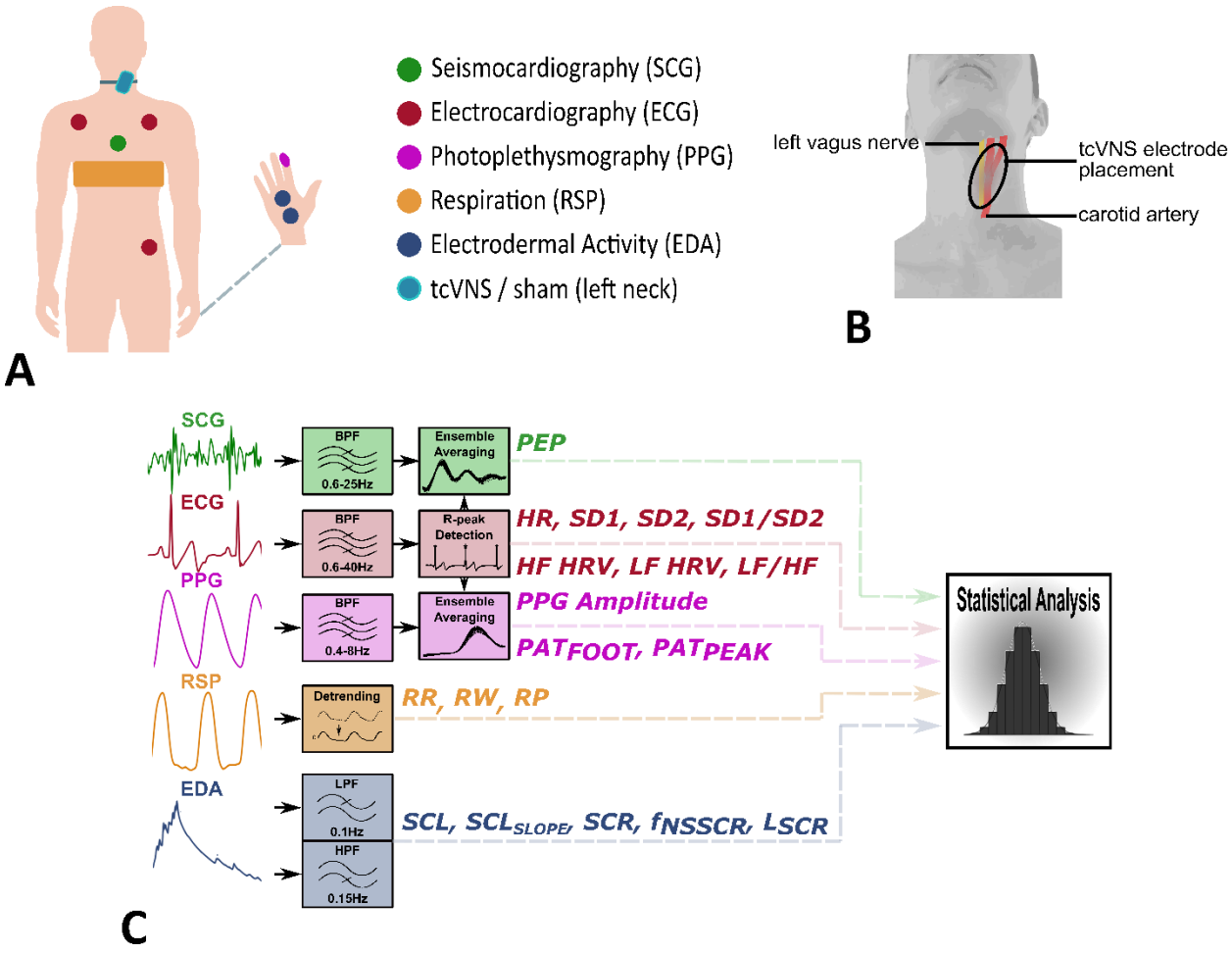
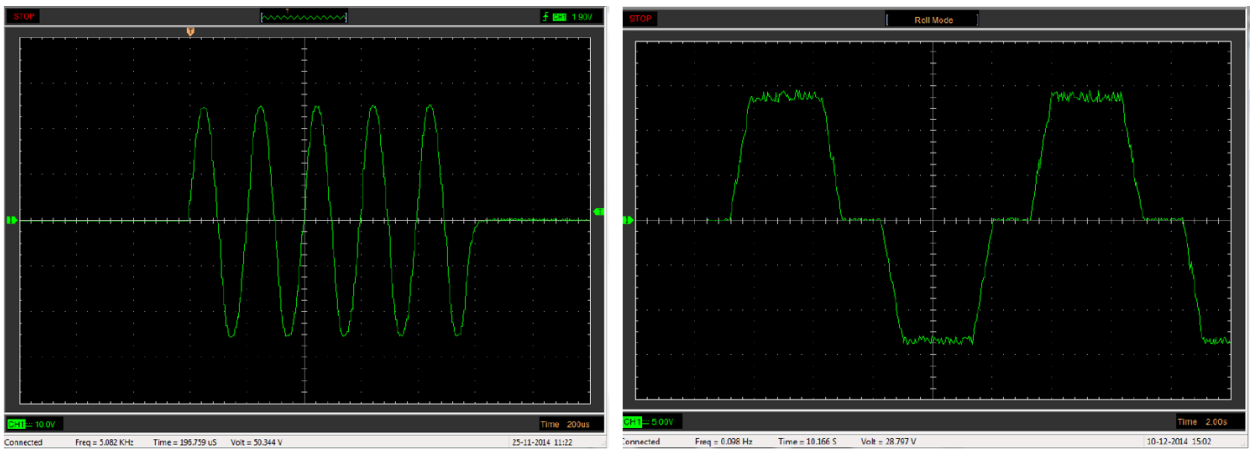


Figure S3. Data collection and signal processing summary. **(A)** Non-invasive sensing modalities shown on participant, active or sham stimulation was applied from left neck. **(B)** Representation of relative locations of left carotid arteries and left vagus nerve. tcVNS electrodes were placed onto the area where the carotid pulsation was located. **(C)** Signal processing and feature extraction summary.



Active: 25 Hz with 5kHz bursts, sine, 30V (peak), 60mA (peak)

Sham: 0.2 Hz, biphasic, 14V (peak), 30mA (peak)

Figure S4. Active tcVNS (left) and sham (right) waveform characteristics as plotted from oscilloscope. The active tcVNS produces an AC electrical signal consisting of five 5,000 Hz pulses (200 microseconds each), repeating at a rate of 25 Hz (once every 40 milliseconds), at 30V (peak) amplitude. The waveform of active pulse is approximately a sine wave. The sham produces an electrical signal consisting of 0.2 Hz pulses, repeating at a rate of every 5 seconds. The waveform of the sham consists of 2 seconds at +14V (peak) then 1 second at 0V then 2 seconds at -14V (peak) approximately in a stepped wave pattern. Both devices have identical placement and operation, both devices stop automatically after 2 minutes. The researcher increases the stimulation intensity to the maximum the participant can tolerate, without pain, regardless of the device type.

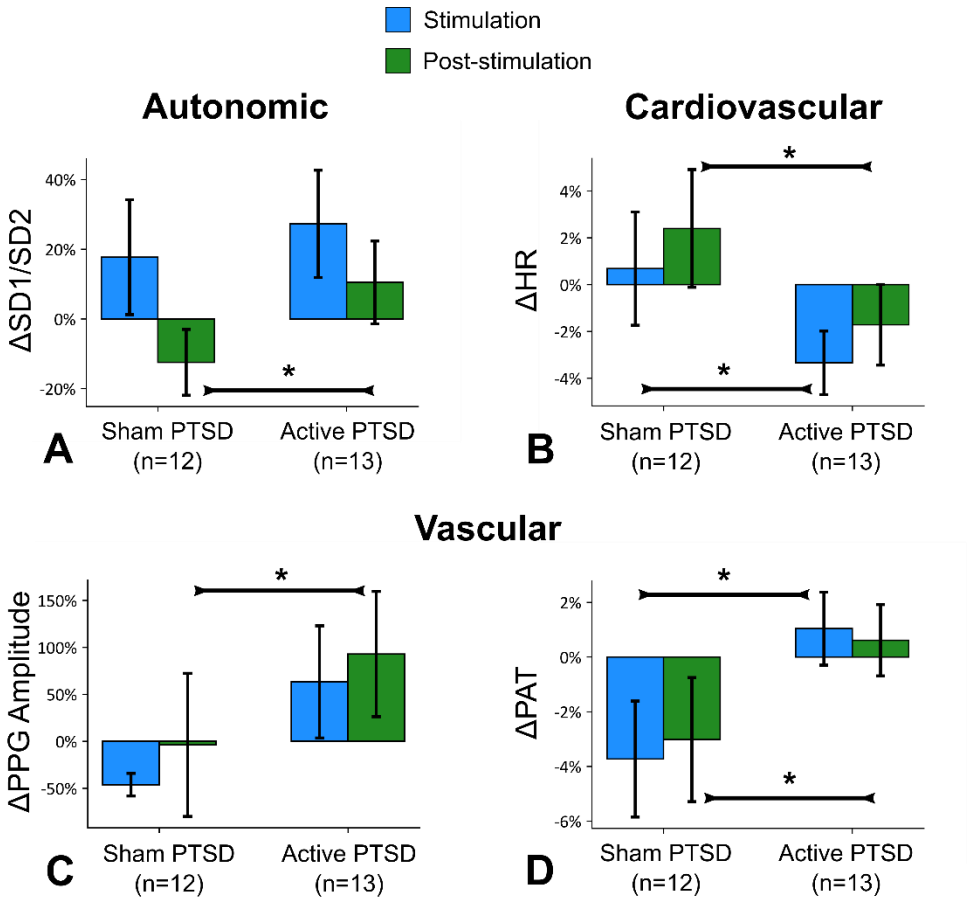


Figure S5. **tcVNS without acute stress, data from the first day.** Bars represent the unadjusted mean changes from baseline, error bars: 95% confidence interval (CI), values calculated from raw data, * indicates p<0.05. ß coefficients, adjusted CI, effect sizes (d), and p-values were reported in ß (±CI, d, p) format. Active tcVNS group experienced the following relative to sham after adjustments: **(A)** Increase in SD1/SD2 following stimulation by 21.9% (±21.9%, d=0.90, p=0.048). **(B)** Decrease in heart rate (HR) during stimulation by 3.9% (±3.7%, d=0.85, p=0.023), and following stimulation by 4.3% (±4.2%, d=0.78, p=0.035). **(C)** Photoplethysmography (PPG) amplitude increased following stimulation by 121.2% (±112.5%, d=0.54, p=0.047). **(D)** Pulse arrival time

(PAT) increased during stimulation by 4.9% (±3.1%, d=1.10, p=0.003), and following stimulation by 3.8% (±3.4%, d=0.81, p=0.023).

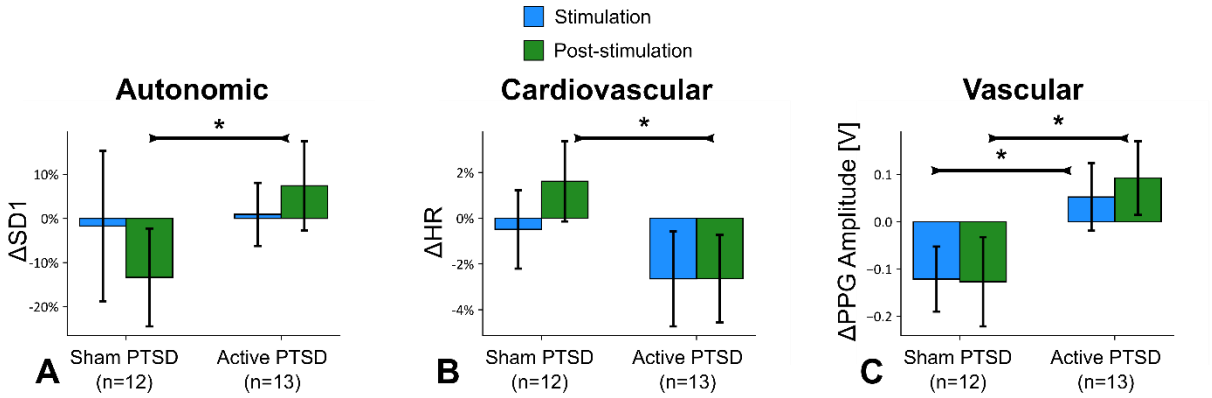


Figure S6. **tcVNS without acute stress, data from the second and third days.** Bars represent the unadjusted mean changes from baseline, error bars: 95% confidence interval (CI), values calculated from raw data, * indicates $p<0.05$. ß coefficients, adjusted CI, effect sizes (d), and p-values were reported in ß (±CI, d, p) format. Active tcVNS group experienced the following relative to sham after adjustments: **(A)** Short-term-variability (SD1) increased following stimulation by 20.3% (±16.5%, d=0.84, p=0.018) **(C)** Heart rate (HR) decreased following stimulation by 4% (±2.9%, d=0.46, p=0.007). **(C)** Photoplethysmography (PPG) amplitude increased during stimulation by 0.18a.u. (±0.1a.u., d=1.01, p=0.004), and following stimulation by 0.23a.u. (±0.1a.u., d=1.03, p=0.003).

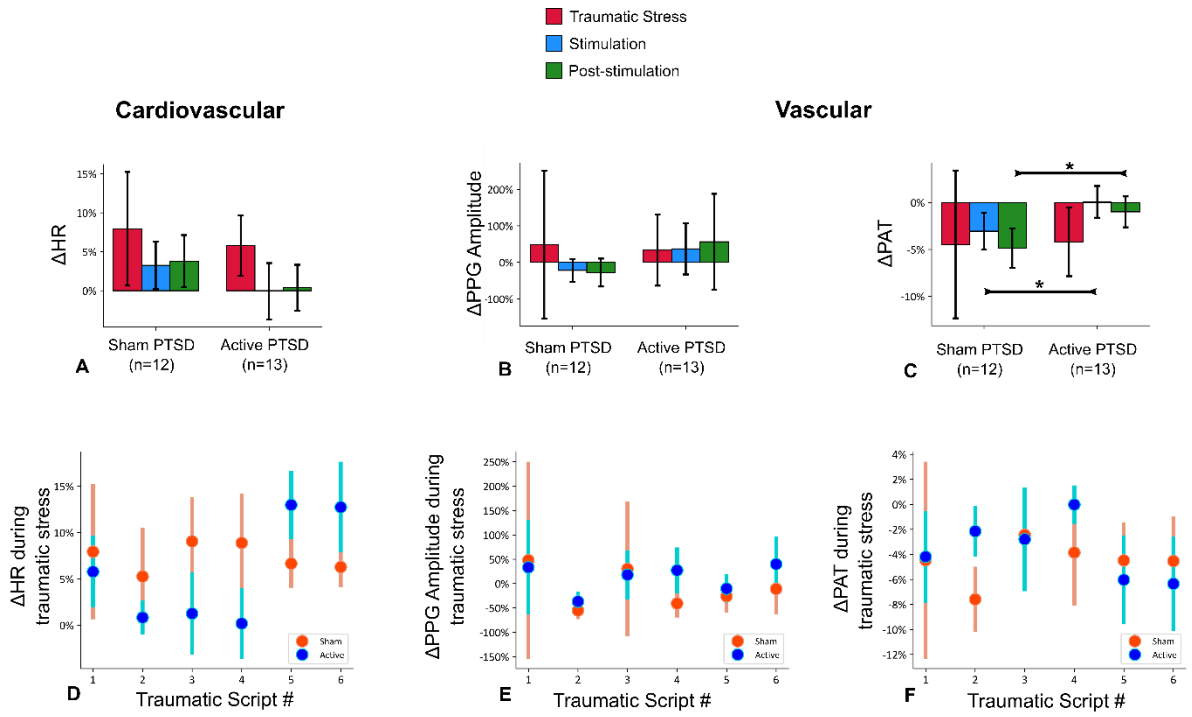


Figure S7. Unadjusted mean changes with ± 95% confidence interval (CI), for the first traumatic stress script and the change in traumatic stress reactivity (or habituation) from the first to the sixth script between the groups (D-F). * indicates p<0.05. ß coefficients, adjusted CI, effect sizes (d), and p-values were reported in ß (±CI, d, p) format. **(A)** No significant difference in heart rate (HR) between groups in any of the intervals. **(B)** No significant difference in photoplethysmography (PPG) amplitude between groups in any of the intervals. **(C)** Pulse arrival time (PAT) increased during stimulation by 3.3% (±2.9%, d=0.95, p=0.027), and following stimulation by 4.2% (±2.9%, d=1.15, p=0.005) after adjustments indicating attenuation in the elevated autonomic tone due to stress. **(D)** HR reactivity to traumatic stress scripts as the protocol transitions from the first to the sixth script. **(E)** PPG amplitude reactivity. **(F)** PAT reactivity.

SUPPLEMENTARY TABLES

ID Number	Device Type	Age [years]	Sex [F/M]	Height [cm]	Weight [kg]	BMI [kg/m^2]
1	active	22	F	165.1	59.0	21.6
2	active	27	F	154.9	57.6	24.0
3	active	34	F	172.7	59.0	19.8
4	active	23	F	170.2	112.5	38.8
5	active	25	F	170.2	58.1	20.0
6	active	42	F	166.4	58.1	21.0
7	active	55	F	165.1	90.7	33.3
8	active	49	F	165.1	73.0	26.8
9	active	19	F	165.1	81.6	29.9
10	active	45	M	193.0	108.9	29.2
11	active	21	F	157.5	65.8	26.5
12	active	23	F	160.0	54.4	21.3
13	active	45	F	177.8	137.0	43.3
14	sham	29	M	182.9	106.6	31.9
15	sham	46	F	167.6	70.3	25.0
16	sham	25	F	154.9	63.5	26.4
17	sham	32	M	177.8	108.9	34.4
18	sham	30	M	188.0	123.8	35.0
19	sham	47	F	162.6	81.6	30.9
20	sham	42	F	180.3	127.0	39.0
21	sham	26	F	175.3	68.0	22.1
22	sham	22	M	180.3	93.0	28.6
23	sham	40	F	160.0	68.0	26.6
24	sham	70	M	185.4	93.0	27.0
25	sham	42	F	154.9	63.5	26.5

Table. S1. Anthropometric information per participant. F, female; M, male; BMI, body mass index.

ID Number	Dx2	Dx3	Dx4	Dx5	Dx6
1	Past MDD	Past SIAD	N/A	N/A	N/A
2	Past alcohol abuse	Past substance abuse	N/A	N/A	N/A
3	N/A	N/A	N/A	N/A	N/A
4	N/A	N/A	N/A	N/A	N/A
5	Panic disorder	N/A	N/A	N/A	N/A
6	Past MDD	Panic disorder	Agoraphobia without panic disorder	Social phobia	GAD
7	Current MDD	N/A	N/A	N/A	N/A
8	N/A	N/A	N/A	N/A	N/A
9	Current MDD	GAD	N/A	N/A	N/A
10	Current MDD	Social phobia	Body dysmorphia	N/A	N/A
11	Past MDD	GAD	Panic disorder	N/A	N/A
12	N/A	N/A	N/A	N/A	N/A
13	N/A	N/A	N/A	N/A	N/A
14	Past alcohol abuse	N/A	N/A	N/A	N/A
15	N/A	N/A	N/A	N/A	N/A
16	Past MDD	N/A	N/A	N/A	N/A
17	Past MDD	N/A	N/A	N/A	N/A
18	N/A	N/A	N/A	N/A	N/A
19	Current MDD	GAD	N/A	N/A	N/A
20	GAD	Panic disorder	N/A	N/A	N/A
21	Past MDD	Current OCD	GAD	N/A	N/A
22	Past MDD	GAD	Panic disorder	N/A	N/A
23	N/A	N/A	N/A	N/A	N/A
24	N/A	N/A	N/A	N/A	N/A
25	N/A	N/A	N/A	N/A	N/A

Table. S2. Comorbid or past diagnosis information per participant. Dx2-6, Comorbid or past diagnoses in addition to PTSD due to SCID; MDD, Major Depressive Disorder; SIAD, Substance Induced Anxiety Disorder; GAD, Generalized Anxiety Disorder; OCD, Obsessive Compulsive Disorder.

Parameter	Active	Sham	P
Age [years]	33.1 (12.0)	37.6 (12.8)	0.21
Sex [F, %]	12F, 92.3%	7F, 58.3%	0.06
Height [cm]	167.9 (9.3)	172.5 (11.4)	0.31
Weight [kg]	78.1 (25.5)	88.9 (22.3)	0.13
BMI [kg/m^2]	27.3 (7.1)	29.5 (4.7)	0.42
HR [bpm]	74.4 (10.9)	68.8 (11.0)	0.23
PEP [ms]	77.5 (55.0)	80.6 (34.5)	0.87
PPG [V]	0.3 (0.3)	0.3 (0.3)	0.57
RR [rpm]	16.9 (3.8)	17.5 (4.5)	0.71
RW [s]	2.0 (0.6)	1.8 (0.5)	0.32
RP [V]	0.7 (0.8)	0.7 (0.9)	0.72
PAT [ms]	264.2 (15.1)	272.8 (11.6)	0.14
HF HRV [ms^2]	611.7 (532.0)	879.9 (668.3)	0.35
LF HRV [ms^2]	738.4 (645.2)	799.5 (529.9)	0.60
LF/HF [n.u.]	1.7 (1.4)	1.2 (0.8)	0.58
SD1 [ms]	22.7 (15.0)	27.0 (13.0)	0.48
SD2 [ms]	57.9 (25.2)	64.7 (22.0)	0.51
SD1/SD2 [a.u.]	378.9 (160.0)	405.2 (113.7)	0.67
SBP [mmHg]	126.8 (22.2)	130.4 (17.1)	0.57
DBP [mmHg]	77.5 (13.6)	74.8 (9.1)	0.79
PP [mmHg]	49.4 (10.8)	55.7 (12.0)	0.25
SCL_{MEAN} [µS]	2.9 (2.9)	4.3 (6.1)	0.50
SCL_{SLOPE}[µS/s]	0.3 (0.7)	3.5 (8.5)	0.12
f_{NSSCR} [pks/s]	0.4 (0.3)	0.4 (0.3)	0.97
L_{SCR} [s]	15.5 (8.7)	24.1 (19.3)	0.62

Table. S3. Anthropometric and physiological parameter information per device group. P: p-value for the comparison between groups.

Traumatic Stress Reactivity [%]	Active [%]	Sham [%]	P
HR	0.06 (0.07)	0.08 (0.13)	0.41
PEP	-0.03 (0.08)	-0.03 (0.06)	0.92
PPG Amplitude	0.33 (1.79)	0.48 (3.58)	0.95
RR	0.17 (0.34)	0.26 (0.41)	0.67
RW	-0.15 (0.17)	0.06 (0.53)	0.11
RP	0.27 (0.56)	0.45 (1.03)	0.70
PAT_{FOOT}	-0.04 (0.07)	-0.04 (0.14)	0.58
PAT_{PEAK}	-0.01 (0.08)	-0.03 (0.13)	0.93
HF HRV	0.16 (0.73)	-0.11 (0.51)	0.37
LF HRV	0.12 (0.74)	-0.12 (0.48)	0.34
LF/HF	0.19 (0.69)	0.90 (1.97)	0.31
SD1	-0.08 (0.38)	-0.06 (0.41)	0.90
SD2	0.10 (0.34)	-0.07 (0.21)	0.25
SD1/SD2	-0.15 (0.27)	0.01 (0.37)	0.33
SBP	0.05 (0.08)	0.03 (0.04)	0.39
DBP	0.05 (0.07)	0.02 (0.08)	0.51
PP	0.06 (0.21)	0.04 (0.17)	0.73
SCL_{MEAN}	0.01 (0.32)	0.06 (0.39)	0.57
SCL_{SLOPE}	-1.63 (10.99)	-1.56 (17.16)	0.94
f_{NSSCR}	0.01 (0.32)	0.06 (0.40)	0.59

Table. S4. First traumatic stress reactivity comparing device groups, before any stimulation happened. Mean (SD) values represent the percent changes due to traumatic stress from baseline. P: p-value for the comparison between groups.

tcVNS paired with traumatic stress (stimulation, post-stimulation)						
	HR	**PPG Amplitude**	**PAT**	**PEP**	**SCL_{SLOPE}**	**RR**
PTSD	0.43, 0.29	0.66, 0.35	0.42, 0.57	0.55, 0.48	0.22, 0.26	0.12, 0.38
Non-PTSD	0.37, 0.33	0.12, 0.19	0.03, 0.14	0.34, 0.40	0.05, 0.05	0.18, 0.28
tcVNS without stress (stimulation, post-stimulation)						
PTSD	0.03, 0.34	0.64, 0.55	0.26, 0.13	0.52, 0.08	0.29, 0.21	0.18, 0.17
Non-PTSD	0.50, 0.55	0.24, 0.34	0.47, 0.42	0.26, 0.35	0.37, 0.13	0.04, 0.12
tcVNS paired with public speech (stimulation, post-stimulation)						
PTSD	0.07, 0.13	0.45, 0.32	0.20, 0.10	0.05, 0.16	0.30, 0.27	0.60, 0.30
Non-PTSD	0.31, 0.26	0.11, 0.03	0.18, 0.05	0.14, 0.16	0.65, 0.03	0.01, 0.5
tcVNS paired with mental arithmetic (stimulation, post-stimulation)						
PTSD	0.52, 0.35	0.40, 0.39	0.13, 0.39	0.14, 0.11	0.30, 0.30	0.14, 0.39
Non-PTSD	0.32, 0.29	0.60, 0.12	0.09, 0.12	0.04, 0.12	0.24, 0.16	0.56, 0.58

Table. S5. Effect size comparisons between PTSD and non-PTSD groups for parameters in both groups. Numbers represent effect sizes (based on Cohen's d) during stimulation and post-stimulation, respectively.