

Supplemental Material

Restoration of somatosensory function by pairing vagus nerve stimulation with tactile rehabilitation

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Table 1. Right (injured) forelimb withdrawal threshold

Animal ID	Group	Week												
		-1	8	16	17	18	19	20	21	22	24	26	28	30
1	Rehab	7.33	29.40	30.50	27.90	23.80	23.20	18.60	24.10	20.90	23.30	25.40	22.40	25.00
2	Rehab	6.17	31.10	28.80	27.50	23.50	21.50	23.60	19.50	19.50	26.60	27.00	27.40	23.60
3	Rehab	10.33	27.33	26.40	25.40	22.50	28.70	27.60	22.30	23.30	23.90	25.30	30.70	22.50
4	Rehab	7.17	26.00	24.50	21.20	23.60	20.50	22.60	23.00	23.30	25.80	26.90	25.00	22.00
5	Rehab	7.75	28.17	26.50	24.80	22.50	23.90	21.10	19.30	22.10	23.30	20.70	21.70	22.80
6	Rehab	8.10	29.17	25.52	20.70	26.20	25.90	25.30	28.60	25.10	24.30	23.60	23.50	23.10
7	Rehab	10.70	31.67	32.80	28.30	26.90	26.90	28.70	25.60	26.80	23.20	25.00	25.60	26.20
8	Rehab	8.30	23.50	22.80	23.00	20.90	21.00	25.60	24.60	25.70	23.70	23.00	23.70	24.70
9	VNS+Rehab	8.00	32.10	29.20	26.50	23.80	11.40	18.20	8.20	9.30	10.50	7.60	13.40	5.00
10	VNS+Rehab	9.67	28.00	25.52	13.70	11.50	6.50	6.40	10.20	11.40	10.70	12.20	12.70	7.60
11	VNS+Rehab	5.83	26.83	24.60	14.80	12.20	17.60	12.50	11.30	12.00	11.10	11.50	12.70	8.90
12	VNS+Rehab	7.17	24.83	23.80	12.70	19.00	11.20	9.00	7.00	13.40	6.70	10.80	6.50	6.60
13	VNS+Rehab	7.50	27.00	27.42	15.90	12.00	14.10	12.50	11.50	11.80	13.20	11.00	10.70	10.10
14	VNS+Rehab	9.26	31.00	28.40	14.20	12.70	15.00	11.10	6.20	12.40	8.80	11.10	9.50	9.70
15	VNS+Rehab	10.76	32.33	28.08	15.90	14.30	11.90	7.50	9.90	9.90	5.60	6.10	8.60	9.30
16	VNS+Rehab	9.70	24.50	29.70	15.40	15.20	11.50	8.90	7.70	9.60	10.00	9.60	11.60	10.70
17	VNS+Rehab	5.90	27.00	28.40	13.60	14.40	12.40	8.10	7.50	9.60	11.70	7.50	9.10	9.20
†18	VNS+Rehab	6.7	29.4	32.1	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
†19	VNS+Rehab	6.83	24.84	26.4	17.5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
†20	VNS+Rehab	8.67	27	31.1	18.4	19.1	22.5	24.1	21.8	25.8	n.d.	n.d.	n.d.	n.d.
†21	VNS+Rehab	6.5	23.5	23.5	22.6	30.4	25.4	27.2	22.3	29.4	n.d.	n.d.	n.d.	n.d.

All forces in grams. † indicates subjects that were excluded from the study for VNS device failure (see Methods). n.d. indicates missing data from time points after exclusion for these subjects.

Table 2. Intent to Treat analysis of injured forelimb withdrawal thresholds

	Week								
Group	-1	8	16	17	18	19	20	21	22
Rehab	8.23±0.55	28.29±0.95	27.23±1.16	24.85±1.06	23.74±0.70	23.95±1.06	24.14±1.19	23.38±1.10	23.34±0.89
VNS+Rehab	7.88±0.44	27.57±0.81	26.55±0.75	16.77±1.18	16.88±1.78	14.50±1.65	13.23±2.10	11.24±1.70	14.05±2.08
p-value	0.63	0.57	0.81	1.41 x 10 ⁻⁴	5.39 x 10 ⁻³	3.74 x 10 ⁻⁴	7.91 x 10 ⁻⁴	3.88 x 10 ⁻⁵	2.08 x 10 ⁻³

ITT analysis including all subjects from Table 1. Data are mean ± SEM. P values represent an unpaired t-test across groups at each time point.

Table 3. Left (uninjured) forelimb withdrawal threshold

Animal ID	Group	Week												
		-1	8	16	17	18	19	20	21	22	24	26	28	30
1	Rehab	8.00	11.50	7.80	6.80	8.80	8.90	11.40	5.30	5.00	8.60	6.10	5.30	5.90
2	Rehab	6.50	10.34	10.90	6.50	9.40	10.60	5.70	6.50	6.60	8.70	6.70	5.50	5.60
3	Rehab	7.00	10.00	7.60	7.30	9.10	11.60	14.40	5.50	13.60	6.70	7.40	6.20	5.20
4	Rehab	8.33	6.50	10.40	10.10	10.50	8.90	6.50	6.80	9.30	6.40	7.50	6.90	9.10
5	Rehab	6.00	9.83	9.82	11.60	10.10	8.40	11.80	4.50	5.00	6.10	5.80	6.90	7.30
6	Rehab	9.80	5.00	9.80	10.10	8.60	9.50	6.70	7.90	7.30	7.10	12.80	7.60	5.70
7	Rehab	10.54	6.00	9.70	10.10	7.90	10.30	4.90	5.30	8.20	6.40	6.90	6.90	7.10
8	Rehab	8.50	4.67	7.40	8.10	8.50	9.90	6.40	10.90	8.60	13.60	8.80	5.30	8.30
9	VNS+Rehab	7.33	8.80	7.40	10.20	9.50	8.10	14.10	14.70	5.10	8.40	6.50	4.50	6.90
10	VNS+Rehab	8.83	10.17	4.50	8.40	10.10	4.40	6.90	7.10	7.70	7.00	5.80	5.20	6.50
11	VNS+Rehab	7.00	7.83	10.20	11.20	9.30	14.40	5.30	8.80	9.40	6.70	8.30	6.70	7.90
12	VNS+Rehab	8.50	8.33	6.70	8.30	7.70	4.20	3.30	6.50	4.50	7.70	5.10	6.30	11.40
13	VNS+Rehab	6.50	5.00	7.00	10.30	6.20	5.50	9.60	15.20	12.80	6.60	5.70	5.80	7.60
14	VNS+Rehab	10.50	5.67	10.80	5.20	5.90	11.70	6.50	4.80	8.50	5.80	5.20	8.50	6.50
15	VNS+Rehab	7.08	6.67	8.10	6.20	3.50	4.30	6.70	6.80	6.50	6.30	7.00	5.60	7.40
16	VNS+Rehab	9.00	7.33	8.00	8.00	7.50	4.10	9.80	5.10	8.20	8.00	10.30	10.80	10.60
17	VNS+Rehab	8.10	6.00	9.40	8.70	6.40	12.40	7.40	6.50	5.90	8.30	9.40	5.30	6.80

All forces in grams

Table 4. Percentage right paw use on the cylinder task

Animal ID	Group	Week						
		-1	16	22	24	26	28	30
1	Rehab	43.0%	31.4%	30.8%	38.8%	35.4%	35.4%	32.3%
2	Rehab	44.3%	19.2%	8.3%	25.0%	16.7%	16.7%	0.0%
3	Rehab	53.1%	33.3%	34.4%	31.3%	36.4%	36.4%	41.7%
4	Rehab	46.9%	22.6%	30.4%	40.0%	38.5%	33.3%	44.4%
5	Rehab	46.6%	27.5%	33.3%	40.0%	31.3%	29.7%	35.3%
6	Rehab	50.3%	30.6%	35.1%	37.3%	26.7%	36.8%	21.2%
7	Rehab	43.8%	25.0%	21.4%	22.2%	25.0%	0.0%	31.3%
8	Rehab	48.3%	25.0%	35.0%	41.4%	14.3%	16.7%	28.6%
9	VNS+Rehab	51.2%	28.8%	56.3%	57.1%	54.5%	53.8%	45.2%
10	VNS+Rehab	50.0%	27.1%	43.1%	42.9%	47.6%	47.1%	46.2%
11	VNS+Rehab	42.9%	36.4%	46.2%	44.8%	31.6%	43.5%	44.4%
12	VNS+Rehab	50.4%	31.3%	49.0%	40.0%	57.1%	57.1%	33.3%
13	VNS+Rehab	52.4%	34.3%	56.3%	60.0%	52.2%	53.8%	41.2%
14	VNS+Rehab	44.0%	35.9%	50.0%	47.5%	44.0%	43.6%	41.4%
15	VNS+Rehab	50.4%	23.1%	43.8%	58.3%	50.0%	42.9%	50.0%
16	VNS+Rehab	42.1%	31.3%	50.0%	41.7%	36.4%	33.3%	33.3%
17	VNS+Rehab	52.3%	28.6%	61.1%	49.2%	50.9%	53.1%	53.4%

Table 5. Right forepaw grip strength

Animal ID	Group	Week						
		-1	16	22	24	26	28	30
1	Rehab	848.15	192.26	118.64	33.21	466.68	508.05	511.91
2	Rehab	855.45	299.96	12.87	26.57	496.90	630.42	692.04
3	Rehab	499.45	115.43	42.39	69.21	433.03	479.12	503.98
4	Rehab	945.48	205.11	261.40	311.92	414.81	398.16	442.74
5	Rehab	501.45	216.80	73.67	344.04	108.87	385.74	276.51
6	Rehab	955.16	122.42	229.62	137.11	330.89	171.41	258.99
7	Rehab	571.29	176.10	214.97	459.07	389.89	354.78	395.63
8	Rehab	477.48	281.82	237.56	420.27	415.15	464.15	371.28
9	VNS+Rehab	885.14	223.79	89.15	25.56	550.74	553.74	591.18
10	VNS+Rehab	855.10	291.30	382.90	404.20	441.44	431.19	414.15
11	VNS+Rehab	912.15	351.60	381.61	618.82	759.22	608.47	636.27
12	VNS+Rehab	814.45	205.15	379.30	382.72	477.39	411.37	383.39
13	VNS+Rehab	515.15	324.81	19.11	55.27	17.81	55.13	129.09
14	VNS+Rehab	845.15	88.98	268.66	51.83	293.20	273.89	249.27
15	VNS+Rehab	405.06	45.00	278.15	484.41	445.94	391.01	447.34
16	VNS+Rehab	515.09	23.93	290.75	272.28	423.61	399.36	519.87
17	VNS+Rehab	489.26	248.16	244.63	221.33	232.24	248.21	310.33

All forces in grams

Table 6. Forepaw toe spread distance

Animal ID	Group	Left	Right
1	Rehab	16.9	11.1
2	Rehab	19.6	11.0
3	Rehab	20.2	13.4
4	Rehab	19.9	12.5
5	Rehab	19.4	13.0
6	Rehab	19.2	9.7
7	Rehab	18.0	10.9
8	Rehab	16.4	13.2
9	VNS+Rehab	19.6	15.9
10	VNS+Rehab	19.2	14.1
11	VNS+Rehab	17.7	13.6
12	VNS+Rehab	19.7	15.2
13	VNS+Rehab	19.9	15.4
14	VNS+Rehab	19.6	13.9
15	VNS+Rehab	19.7	17.1
16	VNS+Rehab	16.9	14.6
17	VNS+Rehab	‡	‡

All distances in mm; ‡ denotes missing data due to technical issues

Table 7. Percentage of steps with slips or misses on the horizontal ladder task

Animal ID	Group	
1	Rehab	29.6%
2	Rehab	16.7%
3	Rehab	15.9%
4	Rehab	16.5%
5	Rehab	19.4%
6	Rehab	25.4%
7	Rehab	20.6%
8	Rehab	23.5%
9	VNS+Rehab	2.2%
10	VNS+Rehab	4.4%
11	VNS+Rehab	6.3%
12	VNS+Rehab	7.4%
13	VNS+Rehab	18.1%
14	VNS+Rehab	11.4%
15	VNS+Rehab	13.2%
16	VNS+Rehab	7.0%
17	VNS+Rehab	4.8%

Video S1. Delivery of Tactile Rehabilitation

Example of the delivery of all four tactile stimuli used during tactile rehabilitation. The animal on the left is receiving VNS paired with tactile rehabilitation while the animal on the right is receiving tactile rehabilitation alone. The VNS indicator turns yellow when VNS is delivered.