Experimental Results/Details of Chronically Cuffed Cervical Vagus Nerve on Rats

Name new Stimulation? Medual RV (not cuffed) Medual RV (not cuffed)	Animal	H&E Histology	Visual Inspection	CNAP Detected in	FG Transport to	FG Transport to	Cytokine Analysis	Days
Instrume Instrume Instrume Instrume Instrume Briefs Not lobserved N/A (cortrol) N/A (cortrol) N/A (cortrol) N/A (cortrol) Cortrol (not device) 22. Briefs Not lobserved N/A (not culled) N/A (cortrol) N/A (cortrol) Cortrol (not device) 22. Briefs Not lobserved N/A (not culled) N/A (cortrol) N/A (cortrol) Cortrol (not device) 23. Briefs Not lobserved N/A (not culled) N/A (dommy device) Expected transport Borned transport Cortrol (dommy device) 23. Briefs Not lobserved N/A (dommy bescap) Expected transport Borned transport Cortrol (dommy device) 17. Briefs Not lobserved N/A (domny bescap) Expected transport Borned transport N/A (do not lobserved) 17. Briefs Not lobserved N/A (domny bescap) Expected transport Borned transport N/A (do not lobserved) 17. Briefs N/A (do not lobserved) N/A (do not lobserved) N/A (do not lobserved) N/A (do not lobse	Name		*	Stimulation?	Medulla RV (not	Medulla LV (cuffed)	***	Implanted
bit NA (control) NA (control) NA (control) Control (or defice) NA bits Mot observed NA (control) NA (control) NA (control) Control (dumm) device) 22 bits Mot observed NA (control) NA (control) Expected transport Control (dumm) device) 23 bits Mot observed NA (control) NA (control) Expected transport Control (dumm) device) 23 bits Mot observed NA (control) NA (control) Expected transport Control (dumm) device) 23 bits Mot observed NA (control) NA (dumm) teadcap) Expected transport Expected transport Control (dumm, device) 17 bits Mot observed NA (control) NA (control) Expected transport Control (no media in cull) 32 bits Mot observed NA (control) NA (control) Expected transport Control (no media in cull) 32 bits Mot observed NA (control) Expected transport Control (no media in cull) 33 bi					cuffed)	**``´		•
Br853 Nutl Diserved NA (not added) NA (advancy deval) Expected transport Control (not devalce) 22 Br8106 Nutl Diserved NA (not added) NA (advancy devalce) Expected transport Control (dummy devalce) 23 Br8106 Nutl Diserved NA (not added) NA (advancy devalce) Expected transport Control (dummy devalce) 23 Br8106 Nutl Diserved NA (not added) NA (advancy devalce) Expected transport Control (dummy devalce) 21 Br8116 Nutl Diserved NA (not added) NA (advancy beackap) Expected transport Control (dummy devalce) 17 Br8116 Nutl Diserved NA (not added) NA (not added) 32 Br8127 Namat Severe mystaling NA (not added) 32 Br8127 Normal Severe mystaling NA (not added) 32 Br8127 Namat Severe mystaling NA (not added) 33 Br8128 Normal Severe mystaling NA (not added) 34 Severed transport Control (no melai in cull) 39 Severed trans	eRx62	Not observed	N/A (not cuffed)	N/A (control)	N/A (control)	N/A (control)	Control (no device)	N/A
aktidb Notidbaseved NA (not defid) NA (durmy device) Expected transport Control (durmy device) 23 aktidb Not (not defid) NA (durmy device) Expected transport Control (durmy device) 23 aktidb Not (not defid) NA (durmy device) Expected transport Control (durmy device) 23 aktidb Not (not defid) NA (durmy headcap) Expected transport Control (durmy device) 21 aktidb Not (not defid) NA (nor metal in cuff) Expected transport Control (durmy device) 22 aktidb Moreal Searce metal in cuff) Expected transport Control (nor metal i	eRx63	Not observed	N/A (not cuffed)	N/A (control)	N/A (control)	N/A (control)	Control (no device/LPS)	N/A
Brit OS Not observed NA (not cuffed) NA (dummy device) Expected transport	eRx104	Not observed	N/A (not cuffed)	N/A (dummy device)	Expected transport	Expected transport	Control (dummy device)	22
BA10 bit bissened NA (not ciffied) NA (dummy device) Expected transport Expected tr	eRx105	Not observed	N/A (not cuffed)	N/A (dummy device)	Expected transport	Expected transport	Control (dummy device)	23
Brittin Noti Observed NA (not cuffied) NA (dummy headcap) Expected transport Omplets appression NA (no biod collection) 32 RK128 Normal Bevet angration NA (no metal in cuff) Expected transport Omplets appression Control (no metal in cuff) 38 RK137 Normal Bevet angration NA (no powerd) Expected transport Omplets appression Control (no metal in cuff) 30 9905 Not observed Bevet angration NA (not powerd) Expected transport Complets appression Control (no metal in cuff) 30 9905 Not observed Bevet angration NA (not powerd) Expected transport Complets appression Control (no stimulation) 42 <	eRx106	Not observed	N/A (not cuffed)	N/A (dummy device)	Expected transport	Expected transport	Control (dummy device)	23
eRx114 Not observed N/A (not udred) N/A (dummy headcap) Expected transport Expected transport Control (dummy device) 17 eRx115 Not observed N/A (not udred) N/A (not metal in cuff) Expected transport Expected transport Expected transport Expected transport N/A (no blocd collection) 32 eRx128 Normal Savere migration N/A (no metal in cuff) Expected transport Complete supressup N/A (no blocd collection) 32 eRx128 Normal Savere migration N/A (no transport Complete supressup Complete supressup Control (no metal in cuff) 33 eRx138 Normal Moderate migration N/A (not powered) Expected transport Complete supressup Control (no simulation) 71 9930 Not observed M/A (not powered) Expected transport Complete supressup Control (no simulation) 74 9915 Not observed N/A (not powered) Expected transport Complete supressup Control (no simulation) 74 9915 Not observed Not observed Not observed <td>eRx110</td> <td>Not observed</td> <td>N/A (not cuffed)</td> <td>N/A (dummy headcap)</td> <td>Expected transport</td> <td>Expected transport</td> <td>Control (dummy device)</td> <td>21</td>	eRx110	Not observed	N/A (not cuffed)	N/A (dummy headcap)	Expected transport	Expected transport	Control (dummy device)	21
eRx151 Not observed NA (not cuffed) NA (constant in cuff) Expected transport Expected transport Control (dummy, no LPS) 17 eRx122 Normal Soviet integration NA (no metal in cuff) Expected transport Complete suppression NA (no blocd collection) 32 eRx123 Normal General in cuff) Expected transport Complete suppression Control (no metal in cuff) 33 eRx133 Normal Moderate ingration NA (no metal in cuff) Expected transport Complete suppression Control (no metal in cuff) 30 eRx133 Normal Moderate ingration NA (not powered) Expected transport Complete suppression Control (no simulation) 71 9932 Not observed Moderate ingration NA (not powered) Expected transport Heav suppression Control (no simulation) 42 9915 Not observed not observed No detection / Bad strain Expected transport Complete suppression Control (no simulation) 42 9915 Not observed not observed No detection / Bad strain	eRx114	Not observed	N/A (not cuffed)	N/A (dummy headcap)	Expected transport	Expected transport	Control (dummy device)	17
Bit All Normal Moderate migration NA (no metal in cuff) Expected transport NA (no block collection) 32 Brit 32 Normal Seaver migration NA (no metal in cuff) Expected transport Complete suppression Control (no metal in cuff) 33 Brit 32 Normal Seaver migration NA (no metal in cuff) Expected transport Complete suppression Control (no metal in cuff) 33 Brit 38 Mormal Seaver migration NA (no travel in cuff) Expected transport Complete suppression Control (no metal in cuff) 33 Brit 38 Mormal Seaver migration NA (not powered) Expected transport Complete suppression Control (no stimulation) 71 Brit 38 Not observed Not (not boserved NA (not powered) Expected transport Complete suppression Control (no stimulation) 73 Brit 38 Not observed Not observed Not (not boserved Not (not boserved) Stavet migration Not (no tool collection) 74 Brit 38 Not observed Not observed Not observed Not del	eRx115	Not observed	N/A (not cuffed)	N/A (dummy headcap)	Expected transport	Expected transport	Control (dummy, no LPS)	17
Brand Severe migration NA fino metal in cuffi Expected transport Complete suppression NA fino metal in cuffi Expected transport Complete suppression Control (no metal in cuff) 33 eRx132 Normal Severe migration NA fino metal in cuffi Expected transport Complete suppression Control (no metal in cuffi 30 eRx133 Normal Severe migration NA fino metal in cuffi Expected transport Complete suppression Control (no metal in cuffi 30 eRx15 Not bisered Moderate migration NA fino powered) Expected transport Complete suppression Control (no simulation) 71 9932 Not observed not observed NA fino powered) Expected transport Complete suppression Control (no simulation) 13 eRx65 Not observed not observed Not detection / bad signal Expected transport Complete suppression Simulated 57 eRx80 Not observed Not detection / bad signal Expected transport Complete suppression Simulated 21 eRx81 Not observed	eRx127	Normal	Moderate migration	N/A (no metal in cuff)	Expected transport	Expected transport	NA (no blood collection)	32
eRx132 Normal Seven migration N/A (no metal in cuff) Expected transport Complete suppression Control (no metal in cuff) 33 eRx137 Normal Seven migration N/A (no metal in cuff) Expected transport Complete suppression Control (no metal in cuff) 30 9809 Not observed Moderate migration N/A (not powered) Expected transport Complete suppression Control (no stimulation) 71 9808 Not observed Sevene migration N/A (not powered) Expected transport Complete suppression Control (no stimulation) 42 eRx66 Not observed not observed No detection/ bad signal Expected transport Complete suppression Stimulated 62 eRx61 Not observed not observed No detection/ bad signal Expected transport Complete suppression Stimulated 62 eRx61 Not observed not observed No detection/ bad signal Expected transport Complete suppression Stimulated 62 eRx61 Not observed not observed No detection / bad signal	eRx128	Normal	Severe migration	N/A (no metal in cuff)	Expected transport	Complete suppression	NA (no blood collection)	32
ERX13 Normal Moderate migration N/A (no metal in cuff) Expected transport Complete suppression Control (no metal in cuff) 30 9803 Not observed Moderate migration N/A (not powered) Expected transport Complete suppression Control (no metal in cuff) 30 9803 Not observed Severe migration N/A (not powered) Expected transport Complete suppression Control (no simulation) 41 9832 Not observed Severe migration N/A (not powered) Expected transport Complete suppression Control (no simulation) 42 98475 Not observed Not detection / bad signal Expected transport Complete suppression Simulated 22 98780 Not observed not observed Not detection / bad signal Expected transport Complete suppression Simulated 21 987811 Not observed	eRx132	Normal	Severe migration	N/A (no metal in cuff)	Expected transport	Complete suppression	Control (no metal in cuff)	38
Pertain Sevent migration N/A (no metal in cuff) Expected transport Complete suppression Control (no metal in cuff) 30 9909 Not observed Severe migration N/A (not powered) Expected transport Complete suppression Control (no stimulation) 42 PRX56 Not observed Severe migration N/A (not powered) Expected transport Heavy suppression Control (no stimulation) 42 PRX56 Not observed Not detection / bad signal Expected transport Complete suppression Stimulated 22 RX63 RX63 Not observed not observed No detection / bad signal Expected transport Complete suppression Stimulat	eRx137	Normal	Moderate migration	N/A (no metal in cuff)	Expected transport	Complete suppression	Control (no metal in cuff)	30
9809 Not observed Moderate migration NA (not powered) Expected transport Complete suppression Control (no stimulation) 71 9932 Not observed Severe migration NA (not powered) Expected transport Complete suppression Control (no stimulation) 42 eRX65 Not observed not observed Not descreed Not descreed A (not powered) Expected transport Complete suppression NA (not boold collection) 45 eRX61 Not observed Not detection / bad signal Expected transport Complete suppression Stimulated 29 eRX63 Not observed not observed Not detection / no recordina Expected transport Complete suppression Stimulated 18 eRX111 Not observed Stimula	eRx138	Normal	Severe migration	N/A (no metal in cuff)	Expected transport	Complete suppression	Control (no metal in cuff)	30
932 Not observed Severe migration N/A (not powered) Expected transport Complete suppression Control (no simulation) 13 6RX6 Not observed	9909	Not observed	Moderate migration	N/A (not powered)	Expected transport	Complete suppression	Control (no stimulation)	71
eRx75 Not observed Severe micration IVA (not powered) Expected transport Heavy suppression Control (no stimulation) 13 eRx66 Not observed not observed Not observed Simulated 57 eRx61 Not observed Not observed Not observed Complete suppression Simulated 62 eRx61 Not observed not observed Not detection / bad sincel Expected transport Complete suppression Simulated 62 eRx63 Not observed not observed No detection / bad sincel Expected transport Complete suppression Simulated 29 eRx64 Not observed not observed No detection / bad sincel Expected transport Complete suppression Simulated 18 eRx64 Not observed not observed No detection / no recording Expected transport Complete suppression Simulated 18 eRx64 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Simulated 48 44 46 <td< td=""><td>9932</td><td>Not observed</td><td>Severe migration</td><td>N/A (not powered)</td><td>Expected transport</td><td>Complete suppression</td><td>Control (no stimulation)</td><td>42</td></td<>	9932	Not observed	Severe migration	N/A (not powered)	Expected transport	Complete suppression	Control (no stimulation)	42
eRx66 Not observed Iso detection / had signal Expected transport Complete suppression NA (no blood collection) 45 9915 Not observed Bevere migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 57 eRx81 Not observed not observed No detection / bad signal Expected transport Complete suppression Stimulated 62 eRx83 Not observed not observed No detection / bad signal Expected transport Complete suppression Stimulated 29 eRx84 Not observed not observed No detection / bad signal Expected transport Complete suppression Stimulated 18 eRx111 Not observed not observed No detector / no recording Expected transport Complete suppression Stimulated 18 eRx63 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 48 9937 Not observed not observed Possible CNAP / ambiguous Expected transport Com	eRx75	Not observed	Severe migration	N/A (not powered)	Expected transport	Heavy suppression	Control (no stimulation)	13
9915 Not observed Severe migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 62 6Rx60 Not observed not observed No detection / bad signal Expected transport Complete suppression Stimulated 62 6Rx80 Not observed not observed No detection / bad signal Expected transport Complete suppression Stimulated 21 6Rx81 Not observed not observed No detection / bad signal Expected transport Complete suppression Stimulated 21 6Rx111 Not observed not observed No detection / no recording Expected transport Complete suppression Stimulated 18 6Rx111 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 18 6Rx64 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 44 6Rx63 Not observed Moderate migration No detection / bad signal Expected transp	eRx66	Not observed	not observed	No detection / bad signal	Expected transport	Complete suppression	NA (no blood collection)	45
eRx61 Not observed Not detection / bad signal Expected transport Complete suppression Stimulated 622 eRx80 Not observed not observed Not detection / bad signal Expected transport Complete suppression Stimulated 29 eRx83 Not observed not observed Not detection / bad signal Expected transport Complete suppression Stimulated 21 eRx111 Not observed not observed Not detection / bad signal Expected transport Complete suppression Stimulated 18 eRx111 Not observed not observed Not detection / to recording Expected transport Complete suppression Stimulated 18 eRx63 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 48 eRx63 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 44 eRx63 Not observed Moderate migration No detection / to ad signal Expected transport Comp	9915	Not observed	Severe migration	Possible CNAP / ambiguous	Expected transport	Complete suppression	Stimulated	57
eRx80 Not observed not observed No detection / bad signal Expected transport Complete suppression Stimulated 97 eRx83 Not observed not observed No detection / bad signal Expected transport Complete suppression Stimulated 29 eRx81 Not observed not observed No detection / bad signal Expected transport Complete suppression Stimulated 18 eRx111 Not observed not observed No detection / basine cavoring Expected transport Complete suppression Stimulated 18 eRx64 Not observed not observed No detection / basine CNAP / ambiguous Expected transport Complete suppression Stimulated 51 9937 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 44 eRx63 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 21 eRx64 Not observed Mod detrate migration No detection / bad signal E	eRx61	Not observed	not observed	No detection / bad signal	Expected transport	Complete suppression	Stimulated	62
eRx83 Not observed not observed No detection / bad signal Expected transport Complete suppression Stimulated 29 eRx84 Not observed not observed No detection / bad signal Expected transport Complete suppression Stimulated 21 eRx111 Not observed not observed No detection / on recording Expected transport Complete suppression Stimulated 18 eRx113 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 48 eRx63 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 48 eRx63 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 44 eRx64 Not observed Moderate migration No detection / no recording Expected transport Complete suppression Stimulated 37 eRx68 Not observed Moderate migration No detection / no recording Expected	eRx80	Not observed	not observed	No detection / bad signal	Expected transport	Complete suppression	Stimulated	37
eRx88 Not observed not observed No detection / bad signal Expected transport Complete suppression Stimulated 21 eRx111 Not observed Severe mitration No detection / no recording Expected transport Complete suppression Stimulated 18 eRx111 Not observed not observed No detection / no recording Expected transport Complete suppression Stimulated 18 eRx64 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 48 eRx55 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 44 eRx63 Not observed Moderate migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 21 eRx118 Not observed Moderate migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 22 eRx1018 Not observed Moderate migration Possible CNAP Expected	eRx83	Not observed	not observed	No detection / bad signal	Expected transport	Complete suppression	Stimulated	29
eRx111 Not observed Severe migration No detection / no recording Expected transport Complete suppression Stimulated 18 eRx111 Not observed not observed No detection / no recording Expected transport Complete suppression Stimulated 51 9937 Not observed Moderate migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 38 9937 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 48 eRx55 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 44 eRx55 Not observed Moderate migration Not detection / no recording Expected transport Complete suppression Stimulated 21 eRx64 Not observed Moderate migration Not detection / no recording Expected transport Complete suppression Stimulated 21 eRx610 Not observed Moderate migration No detection / no recording Expected transport Complete suppression Stimulated 23<	eRx88	Not observed	not observed	No detection / bad signal	Expected transport	Complete suppression	Stimulated	21
eRx113 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 18 9937 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 38 9937 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 48 eRx53 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 44 eRx58 Not observed Moderate migration No detection / bad signal Expected transport Complete suppression Stimulated 21 eRx6113 Not observed Moderate migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 21 eRx6113 Not observed Moderate migration No detection / bad signal Expected transport Complete suppression Stimulated 23 eRx113 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21	eRx111	Not observed	Severe migration	No detection / no recording	Expected transport	Complete suppression	Stimulated	18
eRx64 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 51 9937 Not observed Moderate migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 38 eRx53 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 44 eRx64 Not observed Moderate migration No detection / bad signal Expected transport Complete suppression Stimulated 21 eRx61 Not observed Moderate migration No detection / no recording Expected transport Complete suppression Stimulated 21 eRx102 Not observed Moderate migration No detection / no recording Expected transport Complete suppression Stimulated 23 eRx103 Not observed fot observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx109 Not observed fot observed Conclusive CNAP Expected transport	eRx113	Not observed	not observed	No detection / no recording	Expected transport	Complete suppression	Stimulated	18
9937 Not observed Moderate migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 48 eRx53 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 44 eRx55 Not observed Moderate migration No detection / bad signal Expected transport Complete suppression Stimulated 44 eRx68 Not observed Moderate migration No detection / bad signal Expected transport Complete suppression Stimulated 14 eRx61 Not observed Moderate migration No detection / bad signal Expected transport Complete suppression Stimulated 14 eRx102 Not observed Moderate migration No detection / bad signal Expected transport Complete suppression Stimulated 23 eRx103 Not observed Mod observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx103 Not observed Mot observed Conclusive CNAP Expected transpo	eRx64	Not observed	not observed	Possible CNAP / ambiguous	Expected transport	Complete suppression	Stimulated	51
eRx53 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 44 eRx55 Not observed mot observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 44 eRx68 Not observed Moderate migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 21 eRx61 Not observed Moderate migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 37 eRx118 Not observed mot observed Conclusive CNAP Expected transport Complete suppression Stimulated 23 eRx102 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx108 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx108 Not observed mot observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx101 Not obser	9937	Not observed	Moderate migration	Possible CNAP / ambiguous	Expected transport	Complete suppression	Stimulated	38
eRx55 Not observed not observed Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 44 eRx68 Not observed Moderate migration No detection / bad signal Expected transport Complete suppression Stimulated 21 eRx61 Not observed Moderate migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 37 eRx10 Not observed Moderate migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 37 eRx102 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 23 eRx103 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx103 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx101 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport	eRx53	Not observed	not observed	Possible CNAP / ambiguous	Expected transport	Complete suppression	Stimulated	48
eRx68 Not observed Moderate migration Not detection / bad signal Expected transport Complete suppression Stimulated 21 eRx61 Not observed Moderate migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 37 eRx118 Not observed Moderate migration Not detection / no recording Expected transport Complete suppression Stimulated 14 eRx103 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 23 eRx108 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx109 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx119 Not observed Mild or no migration Not detection / bad signal Expected transport Complete suppression Stimulated 21 eRx119 Not observed Mild or no migration Possible CNAP / ambiguous Expected tran	eRx55	Not observed	not observed	Possible CNAP / ambiguous	Expected transport	Complete suppression	Stimulated	44
eRx81 Not observed Moderate migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 37 eRx118 Not observed Moderate migration No detection / no recording Expected transport Complete suppression Stimulated 14 eRx102 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 23 eRx103 Not observed not observed Conclusive CNAP Expected transport Light suppression Control (no LPS) 22 eRx103 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx103 Not observed Mild or no migration No detection / bad signal Expected transport Complete suppression Stimulated 21 eRx111 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 21 eRx112 Not observed Mild or no migration Possible CNAP / ambiguous Expected t	eRx68	Not observed	Moderate migration	No detection / bad signal	Expected transport	Complete suppression	Stimulated	21
eRx118 Not observed Moderate migration Not detection / no recording Expected transport Complete suppression Stimulated 14 eRx102 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 23 eRx103 Not observed Mild or no migration Conclusive CNAP Expected transport Light suppression Control (no LPS) 22 eRx108 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx101 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx101 Not observed Mild or no migration No detection / bad signal Expected transport Complete suppression Stimulated 44 eRx111 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 13 eRx112 Not observed Mild or no migration Possible CNAP / ambiguous Expected transpo	eRx81	Not observed	Moderate migration	Possible CNAP / ambiguous	Expected transport	Complete suppression	Stimulated	37
eRx102 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 23 eRx103 Not observed Mild or no migration Conclusive CNAP Expected transport Light suppression Stimulated 21 eRx108 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx109 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx101 Not observed Mild or no migration Rodetection / bad signal Expected transport Complete suppression Stimulated 21 eRx111 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 13 eRx111 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 17 eRx112 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 14 eRx	eRx118	Not observed	Moderate migration	No detection / no recording	Expected transport	Complete suppression	Stimulated	14
eRx103 Not observed Mild or no migration Conclusive CNAP Expected transport Light suppression Control (no LPS) 22 eRx108 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx109 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx110 Not observed Mild or no migration No detection / bad signal Expected transport Complete suppression Stimulated 21 eRx71 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 13 eRx111 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Moderate suppression Stimulated 14 eRx112 Normal Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 27 eRx141 Normal Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 26	eRx102	Not observed	not observed	Conclusive CNAP	Expected transport	Complete suppression	Stimulated	23
eRx108 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx109 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx11 Not observed Mild or no migration No detection / bad signal Expected transport Complete suppression Stimulated 21 eRx12 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 13 eRx119 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Heavy suppression Stimulated 14 eRx111 Normal Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 14 eRx114 Normal Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 27 eRx142 Normal Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 26 eRx1	eRx103	Not observed	Mild or no migration	Conclusive CNAP	Expected transport	Light suppression	Control (no LPS)	22
eRx109 Not observed not observed Conclusive CNAP Expected transport Complete suppression Stimulated 21 eRx71 Not observed Mild or no migration No detection / bad signal Expected transport Complete suppression Stimulated 44 eRx71 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 44 eRx116 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Heavy suppression Stimulated 11 eRx111 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Moderate suppression Stimulated 11 eRx141 Normal Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 27 eRx142 Normal Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 26 eRx142 Normal Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 26	eRx108	Not observed	not observed	Conclusive CNAP	Expected transport	Complete suppression	Stimulated	21
eRx71 Not observed Mild or no migration Not detection / bad signal Expected transport Complete suppression Stimulated 44 eRx72 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 13 eRx116 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Heavy suppression Stimulated 17 eRx111 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Moderate suppression Stimulated 14 eRx111 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 27 eRx142 Normal Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 26 eRx142 Normal Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 26 eRx143 Normal Mild or no migration Conclusive CNAP Expected	eRx109	Not observed	not observed	Conclusive CNAP	Expected transport	Complete suppression	Stimulated	21
eRx72 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 13 eRx116 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Heavy suppression Stimulated 17 eRx119 Not observed Mild or no migration No detection / bad signal Expected transport Moderate suppression Stimulated 14 eRx111 Normal Mild or no migration Possible CNAP / ambiguous Expected transport Moderate suppression Stimulated 14 eRx142 Normal Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 26 eRx142 Normal Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 26 eRx143 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx144 Not observed Mild or no migration Conclusive CNAP Expected transport	eRx71	Not observed	Mild or no migration	No detection / bad signal	Expected transport	Complete suppression	Stimulated	44
eRx116 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Heavy suppression Stimulated 17 eRx119 Not observed Mild or no migration No detection / bad signal Expected transport Moderate suppression Stimulated 14 eRx111 Normal Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 27 eRx142 Normal Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 26 eRx143 Normal Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 26 eRx144 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx144 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx144 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36	eRx72	Not observed	Mild or no migration	Possible CNAP / ambiguous	Expected transport	Complete suppression	Stimulated	13
eRx119 Not observed Mild or no migration No detection / bad signal Expected transport Moderate suppression Stimulated 14 eRx111 Normal Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 27 eRx142 Normal Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 26 eRx143 Normal Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 26 eRx144 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx147 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx148 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx150 Not observed Mild or no migration Conclusive CNAP Expected transport	eRx116	Not observed	Mild or no migration	Possible CNAP / ambiguous	Expected transport	Heavy suppression	Stimulated	17
eRx141 Normal Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 27 eRx142 Normal Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 26 eRx143 Normal Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 26 eRx143 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 26 eRx147 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx148 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx150 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx150 Not observed Mild or no migration Conclusive CNAP Expected transport <t< td=""><td>eRx119</td><td>Not observed</td><td>Mild or no migration</td><td>No detection / bad signal</td><td>Expected transport</td><td>Moderate suppression</td><td>Stimulated</td><td>14</td></t<>	eRx119	Not observed	Mild or no migration	No detection / bad signal	Expected transport	Moderate suppression	Stimulated	14
eRx142 Normal Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 26 eRx143 Normal Mild or no migration Possible CNAP Expected transport Complete suppression Stimulated 26 eRx144 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx147 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx148 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx148 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx150 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 34 eRx152 Not observed Mild or no migration Conclusive CNAP Expected transport Comp	eRx141	Normal	Mild or no migration	Possible CNAP / ambiguous	Expected transport	Complete suppression	Stimulated	27
eRx143 Normal Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 26 eRx144 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx147 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx148 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx148 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx150 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 36 eRx152 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 34 eRx152 Not observed Mild or no migration Conclusive CNAP Expected tra	eRx142	Normal	Mild or no migration	Conclusive CNAP	Expected transport	Complete suppression	Stimulated	26
eRx144 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx147 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx148 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx148 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx150 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx152 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 34 eRx152 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Control (no IPS) 34	eRx143	Normal	Mild or no migration	Possible CNAP / ambiguous	Expected transport	Complete suppression	Stimulated	26
eRx147 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx148 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx150 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx150 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 34 eRx152 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 34	eRx144	Not observed	Mild or no migration	Conclusive CNAP	Expected transport	Complete suppression	Stimulated	36
eRx148 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Stimulated 36 eRx150 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 36 eRx152 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 34 eRx152 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Control (no LPS) 34	eRx147	Not observed	Mild or no migration	Conclusive CNAP	Expected transport	Complete suppression	Stimulated	36
eRx150 Not observed Mild or no migration Possible CNAP / ambiguous Expected transport Complete suppression Stimulated 34 eRx152 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Control (no LPS) 34	eRx148	Not observed	Mild or no migration	Conclusive CNAP	Expected transport	Complete suppression	Stimulated	36
eRx152 Not observed Mild or no migration Conclusive CNAP Expected transport Complete suppression Control (no.1.P.S.) 34	eRx150	Not observed	Mild or no migration	Possible CNAP / ambiguous	Expected transport	Complete suppression	Stimulated	34
	eRx152	Not observed	Mild or no migration	Conclusive CNAP	Expected transport	Complete suppression	Control (no LPS)	34

Table illustrates results from chronic testing for 47 rats: Blue = a good or expected result; Red = a bad or unexpected result; Yellow = indeterminant result; White = not tested or not applicable in that animal.

* "Moderate" migration was defined as an electrode(s) that was generally in the correct location but had moved laterally ~1mm or less and/or appeared to have rotated ~30 degrees or less. The nerve still appeared to be intact and encompassed in the cuff electrode. "Severe" was be defined as an electrode(s) that had obvious migrations of >1mm laterally, rotation of >30 degrees, and/or signs of significant pulling or tearing of the encompassed vagus nerve.

** "Heavy" suppression was quantified as having no more than 15 illuminated cells in any given medulla section. "Moderate" suppression was quantified as having more than 15 illuminated cells in any given medulla section, but still had a majority of cells suppressed. "Light" suppression was quantified as having observable cell suppression, but the majority of cells illuminated.

*** Highlighted (green) and italicized items indicate animals that were included in our cytokine analyses.

Experimental Results/Details of Chronically Cuffed Cervical Vagus Nerve on Rats Used for Gastric Emptying Experiments

Animal Name	Control Scan	Stimulation Scan	Necropsy Nerve Inspection	FG Transport to Medulla RV (not	FG Transport to Medulla LV (cuffed)	Medulla FG Brightness	Nodose FG Brightness	Days Implanted
			*	cuffed)	**	-	-	
	Good							
eRx157 ***	Results	N/A	N/A	N/A	N/A	N/A	N/A	23
	Good							
eRx159	Results	Good Results	Mild or no migration	Expected Transport	Heavy Suppression	Bright	Bright	34
	Good	Total Apnia,						
eRx160	Results	Stopped Stim	Mild or no migration	Expected Transport	Moderate Suppression	Bright	Dull But Present	35
	Good	Apnia During						
eRx161	Results	Stim	Mild or no migration	Expected Transport	Complete Suppression	Bright	Bright	47
	Good							
eRx162	Results	Good Results	Mild or no migration	Expected Transport	Moderate Suppression	Bright	Bright	46
	Breathing	Apnia During	Moderate					
eRx163	Issues	Stim	Migration/Pulling	Expected Transport	Complete Suppression	Dull But Present	Dull But Present	48

Table illustrates results from chronic testing for 6 rats: Blue = a good or expected result; Red = a bad or unexpected result; Yellow = indeterminant result; White = not tested or not applicable in that animal.

* "Moderate" migration was defined as an electrode(s) that was generally in the correct location but had moved laterally ~1mm or less and/or appeared to have rotated ~30 degrees or less. The nerve still appeared to be intact and encompassed in the cuff electrode.

** "Heavy" suppression was quantified as having no more than 15 illuminated cells in any given medulla section. "Moderate" suppression was quantified as having more than 15 illuminated cells in any given medulla section, but still had a majority of cells suppressed.

*** eRx157 knocked its headcap off before the scheduled stimulation scan and was euthanized.

Overview of 17 Previous Studies Using Chronic Vagus Nerve Cuffing

Topic			Animals			Cuffs				Tests				Reference
										Done				
Biological Topic	Fiber Target (Afferent / Efferent)	Nerve Cuffed	Breed (Rat)	Weight	Sample Size	Cuff Type	Cuff Inner Diameter	Duration Cuffed	Cuffing Technique	CNAP Recorded	Nerve Histology	Fluorogold Used	Inflammation Measured	Author
Seizure suppression	Afferent	Left	Sprague-Dawley		34			4 days	Nerve isolated (assumed), cuffed	No	No	No	No	Krahl et al. (2001) [22]
Anti-depression	Afferent	Left	Sprague-Dawley	275g+	5-6 per group	Cyberonics helical	1mm (assumed)	2 days + (1 hour to 90 days)	Cuffs wrapped around nerve & carotid; leads suture to muscle	No	No	No	No	Dorr et al. (2006) [23]
Tremor suppression	Afferent	Left	Long-Evans	300- 350g	7	Cyberonics helical	1mm	4+ days	Cuffs wrapped around nerve & carotid	No	No	No	No	Handforth et al. (2001) [24]
Hippocampal neuronal plasticity	Afferent	Left	Sprague-Dawley	250- 300g	6 per group	Cyberonics helical		2 days + 1 month	Cuffs wrapped around nerve & carotid	No	No (Brain)	No	No	Biggio et al. (2009) [25]
Neuroprotective effects in brain	Afferent	Left	Wistar	Variable	24	Cyberonics helical		13 weeks	Cuffs wrapped around nerve (carotid unspecified)	No	No (Brain)	No	Yes (Plasma, brain)	Chunchai et al. (2016) [26]
Brain biomarkers / anti-depression	Afferent	Left	Sprague-Dawley	250- 350g	29	Cyberonics helical		4 weeks	References Dorr et al.	No	No	No	No	Cunningham et al. (2008) [15]
Anti-depression	Afferent	Left	Sprague-Dawley	250- 300g	45	Self-sizing spiral cuff	1mm	8 weeks	Nerve isolated; wrapped with cuff	No	No (Brain)	No	No	Grimonprez et al. (2015) [27]
Body weight / fat mass	Both Possible	Left	Sprague-Dawley	250- 300g	13 max per group	Cyberonics helical		2 days + 4 weeks	Cuffs wrapped around nerve (carotid unspecified)	No	No	No	No	Banni et al. (2012) [72]
Pain memory	Afferent	Left	Sprague-Dawley	300- 350g	8 max per group	PVS sheath	1 mm	16 days	Nerve isolated; pvc around nerve; leads sutured to cleidomastoid	No	No	No	No	Zhang et al. (2013) [28]
Fear / memory conditioning	Afferent	Left	Sprague-Dawley	250- 300g	40	Silicone tube	1 mm	13 days	Nerve isolated; cuffed	No	No	No	No	Pena et al. (2014) [29]
Enhanced memory	Both	Left	Long-Evans	350- 450g	64	PVC sheath	1 mm	~3 days	Nerve isolated; pvc around nerve; leads sutured to cleidomastoid; bone wax inside cuff	Yes	No	No	No	Clark et al. (1998) [14]
Bowel Inflammation	Both	Left	Sprague-Dawley		48	Cyberonics helical		17 days	Cuffs wrapped around nerve & carotid	No	No (Colon)	No	Yes (Colon)	Meregnani et al. (2011) [34]
Cardiac remodeling (heart failure)	Both	Left	Sprague-Dawley		63	Silicone tube	0.75 mm	14 weeks	Nerve isolated; cuffed/sutured shut; strain relief cuff placed around nerve cuff and artery	No	No	No	No	Agarwal et al. (2016) [30]
Hypertension, Cardiovascular damage	Both	Right	Rat (not specified)		24	Wire with Kwik- Sil	wrapped wire	4-5 weeks	Nerve isolated; wire wrapped around; Kwik-Sil encapsulated	No	No	No	Yes (Serum)	Chapleau et al. (2016) [31]
Negative heart impacts	Both	Right	Sprague-Dawley	250- 300g	9	Cyberonics helical	1.5 mm	10 weeks	Cuffs wrapped around nerve & carotid	No	No	No	No	Lee et al. (2016) [32]
Artery pressure / heart rate	Both	Right	Sprague-Dawley	250- 350g		Silicone tube	0.5 mm	up to 3 months	Nerve isolated, cuffed/sutured shut	No	No	No	No	Zheng et al. (2014) [33]
Larynx action potentials	Efferent	Left	Wistar	250- 350g	21 chronic	Self-sizing silicone tube	1 mm	8 weeks	Nerve isolated, cuffed	Yes	No	No	No	El Tahry et al. (2011) [35]
Inflammation / Gastric Emptying	Efferent	Left	Sprague-Dawley	190- 300g	53	Silicone tube	0.75 mm	13-71 days	Nerve isolated, cuffed	Yes	Yes	Yes	Yes (Plasma)	Somann et al (2017)*

*This study included for comparison purposes

Stimulation Details of 17 Previous Studies Using Chronic Vagus Nerve Cuffing

Stimulation Parameters			Stimulation Protocols	3		Additional Stimulation Details		Reference
Amplitude	Pulse Width (μs)	Frequency (Hz)	Pulse Details	Stimulation Duration	Stimulation Timeline	Delivery Mechanism	Stimulation Verification	Author
1 mA	500	20	Square-wave pulses	15 minute continuous pulse train	Half stimulated after 2 days, the remainder after 4 days	-	-	Krahl et al. (2001) [22]
0.25 mA	500	20	-	30 sec on, 5 min off, continuous	1 hour, 1 day, 3 day, 2-week, 3-week, & 3- month VNS groups	Implanted Cyberonics 102 Pulse Stimulator	Lead impedance check, no functional test presented	Dorr et al. (2006) [23]
0.5 mA	500	20	Balanced biphasic	5 min continuous pulse train	4+ day recovery, then 5 consecutive 20 min treatments (5 min baseline, 5 min acute VNS, 10 min post period)	A-M Systems Model 2100 stimulator, tethered to headcap	-	Handforth et al. (2001) [24]
1.5 mA	500	30	-	30 sec on, 5 min off, continuous	2 day recovery, then 3 hour or 1 month VNS	Implanted Cyberonics stimulator	-	Biggio et al. (2009) [25]
0.5 - 0.75 mA	500	20	-	14 sec on, 48 sec off, continuous	1 week recovery, then 12 week VNS	Implanted Cyberonics Demipulse stimulator	-	Chunchai et al. (2016) [26]
0.25 mA	250	20	-	30 sec per 5 min, continuous	1 week recovery, then 2 hour or 3 week VNS	Implanted Cyberonics stimulator	-	Cunningham et al. (2008) [15]
0.25, 0.5, or 1 mA	250	30	-	7 sec on, 18 sec off, continuous	1 week recovery, 5 week baseline, then 2 week VNS	Stimulator tethered to headcap	Daily impedance test with 1mA square wave	Grimonprez et al. (2015) [27]
1.5 mA	500	30	-	30 sec on, 5 min off, continuous	2 day recovery, then 3 hour or 4 week VNS	Implanted Cyberonics Demipulse Model 103 stimulator	Dedicated test pre-implant	Banni et al. (2012) [72]
0.04 or 0.4 mA	500	1	-	30 seconds acute VNS pre or post conditioning	5 day recovery, pre-condition day, then 3 consecutive conditioning days	A-M Systems Model 2100 stimulator, tethered through neck incision	Respiration and behavioral response to VNS	Zhang et al. (2013) [28]
0.4 mA	500	30	-	30 seconds	1 week recovery, then 5 conditioning/ treatment days (acute VNS on day 4)	Tucker Davis Tech. MS4 stimulator, tethered to headcap	Respiration response to 0.2 mA, 60 Hz, 10 sec VNS	Pena et al. (2014) [29]
0.2, 0.4, or 0.8 mA	500	20	Biphasic pulses	30 seconds	2 day recovery, then condition testing with acute VNS	Undefined stimulator, tethered through neck incision	Action potentials recorded	Clark et al. (1998) [14]
1 mA	500	5	-	10 sec on, 90 sec off, continuous	12 day recovery, then 3 hour VNS per day (5 days)	Grass Technologies stimulator chain, tethered through head connector	-	Meregnani et al. (2011) [34]
0.05 - 0.25 mA	200	20	-	10 sec on, 50 sec off, continuous	7 day recovery, then 6 week VNS	Undefined pulse generator and connection.	Respiration and heart rate response	Agarwal et al. (2016) [30]
3 V	1000	5	Charge balanced	1 hour on, 1 hour off, continuous	3-4 day recovery, then 4 week VNS	Implanted Harald Stauss Scientific Model RNS stimulator	Heart rate and blood pressure response	Chapleau et al. (2016) [31]
1 mA	500	20	-	7 sec on, 66 sec off, continuous	10 week VNS	Implanted Cyberonics Demipulse Model 103 stimulator	-	Lee et al. (2016) [32]
0.1 - 1 mA	200	20	Rectangular pulses	Various, intermittent	6 weeks intermittent VNS	Implanted Unimec ISE1000SA pulse generator	Heart rate and artery pressure	Zheng et al. (2014) [33]
0.04 - 0.8 mA	500	-	Block-pulses	Various to determine dose response curves	5 days / week, for 8 weeks	Undefined stimulator tethered to headcap	Action potentials recorded	El Tahry et al. (2011) [35]
Various (1 mA typical)	Various (1 ms typical)	5	Balanced biphasic square pulses	5 - 10 min pre- calibration, 5 min treatment	13 – 71 day recovery, then pre-calibration VNS 30 min before, acute VNS 30 min after endotoxin	Bionode, fully implanted or tethered to headcap	Direct recording, separate recording cuff	Somann et al (2017)*

*This study included for comparison purpose



Supplemental Figure 1. Photograph showing a standard stimulation cuff used in our studies. Threaded wire electrode was used as a grounding reference for stimulation and oriented cranially.



Supplemental Figure 2. Pre-perfusion visual inspection of two animals, both showing cuffs in correct location with vagus nerve intact. (a) From a rat that demonstrated complete suppression of Fluorogold transport (eRx71), while (b) demonstrated a limited but present transport (eRx103).



Supplemental Figure 3. Representative fluorescence images and image mosaics of a single rat (eRx144). (a) medulla image showing clear efferent fiber FG transport on the right side of the dorsal motor nucleus, and complete suppression of transport on the left side. (b1) tissue dissected cranial to stimulation cuff on left vagus nerve, with enhanced image of nodose ganglia (b2) showing FG illumination. (c1) cervical column of right vagus nerve and surrounding tissue, with enhanced image of nodose ganglia (c2) showing FG illumination. Vagus nodose ganglia from each side show similar size, shape, location, and textural illumination, indicating active afferent fiber transport in both despite a complete suppression of efferent fiber transport in the cuffed left vagus. Note that the bright yellow and orange illumination on the upper edge of the carotid artery is from ink residue used to mark the samples during explant and has no bearing on FG illumination.



Supplemental Figure 4. Representative fluorescence images and image mosaics of a single rat (eRx162).
(a) medulla image showing clear efferent fiber FG transport on the right side of the dorsal motor nucleus, and significant suppression of transport on the left side. (b1) cervical column dissected cranial to stimulation cuff on left vagus nerve, with enhanced image of nodose ganglia (b2) showing FG illumination. (c1) cervical column of right vagus nerve and surrounding tissue, with enhanced image of nodose ganglia (c2) showing FG illumination. Vagus nodose ganglia from each side show similar size, shape, location, and textural illumination, indicating similar active afferent fiber transport in both despite a suppression of efferent fiber transport in the cuffed left vagus.



Supplemental Figure 5. Comparative fluorescence images of two separate rats demonstrating healthy FG transport through efferent fibers to the DMN and afferent fibers to the nodose in uncuffed right vagus nerves, but only through afferent fibers in cuffed left vagus nerves. (a) medulla image (from eRx160) showing clear efferent fiber FG illumination on the right side of the dorsal motor nucleus, and severe suppression of FG on the left side. (b & c) corresponding fluorescence nodose images of the cuffed left and uncuffed right (respectively) vagus nerves (from eRx160). (d) medulla image (from eRx162) also showing strong efferent fiber FG illumination on the right side of the dorsal motor nucleus, and significant suppression of FG on the left side. (e & f) corresponding fluorescence nodose images of the cuffed left and uncuffed right (respectively) vagus nerves (from eRx162). Red dashed lines separate the left vagal effects from right vagal effects. Scale bars = 250 microns.

Supplemental methods for hematoxylin and eosin histology

For paraffin processing, nerve tissue was processed in a Sakura VIP6 Tissue Processor. The protocol timing used is shown in Supplemental Table 4. All solutions were used under vacuum pressure and at room temperature, except the paraffin which was infiltrated at 61° C. The tissue was then embedded in Leica Paraplast Plus paraffin and cut on a Leica FinesseME microtome at a thickness of 4 micrometers. Slides were dried in a 60° C oven for an hour and stained in a Shandon Varistain autostainer with Gill's Hematoxylin (3 min.) and Eosin Y/Phloxine B (30 sec.). Stained sections were dehydrated through graded alcohols, cleared in xylene, and coverslipped.

For plastic processing, cuffed nerve tissue was processed in a Leica TP1020 processor using the protocol timing in Supplemental Table 4. All stations, except the Acetone, were used under vacuum. The last two changes of PMMA were done by hand in a glass desiccator under vacuum. All Methyl-MethAcrylate (MMA) changes were a solution of 95% MMA (Fisher Scientific) and 5% Dibutyl Phthalate (Fisher Scientific). The cuffed nerve samples were embedded in prepolymerized molds using a solution of 95% MMA and 5% dibutyl phthalate. 0.25% Perkadox16 was used as an initiator for polymerization. The molds were then left at room temperature for a week to polymerize. After the blocks were fully polymerized, they were put in a 60° C oven for an hour to complete polymerization and evaporate any remaining MMA. The PMMA blocks were then trimmed with a Mar-med band saw and mounted on plastic blocks for sectioning in a Reichert-Jung Polycut S. Sections were taken from the PMMA blocks at a thickness of 4-5 micrometers and mounted on APES (Sigma Aldrich) coated slides. The slides were compressed in a metal press and left in a 60° C oven overnight. The slides were then de-plasticized in three changes of acetone for 10 minutes each, hydrated and stained in a Shandon Varistain autostainer with Gill's Hematoxylin (5 min) and Eosin Y/Phloxine B (2 min.). Stained sections were dehydrated and coverslipped as the paraffin sections.

-	Paraffin Proce	ssing		PMMA Processing				
Station	Solution	Time (min)) Station		Solution	Time (hrs)		
1	10% NBF	0:00		1	70%ETOH	1		
2	70%ETOH	0:05		2	95%ETOH	1		
3	80%ETOH	0:05		3	95%ETOH	1		
4	95%ETOH	0:05		4	100%ETOH	2		
5	95%ETOH	0:05		5	100%ETOH	2		
6	100%ETOH	0:05		6	100%ETOH	3		
7	100%ETOH	0:05		7	Acetone	2		
8	100%ETOH	0:10		8	Acetone	2		
9	XYLENE	0:05		9	MMA 1	12		
10	XYLENE	0:10		10	MMA 2	12		
11	PARAFFIN	0:05		11	MMA 3	12		
12	PARAFFIN	0:05		12	MMA 4	24		
13	PARAFFIN	0:05			Total Time (days)	74		
14	PARAFFIN	0:05						
	Process Time	1:15						
	Total Time	2:15						

Supplemental Table 4

Protocol timing used in paraffin tissue and cuff, and PMMA and cuff sample processing.