

Supplementary Table 1 VNS For Inflammatory Bowel Disease

Subjects		Stimulation Method and Site	Stimulation Parameters	Stimulus Duration	Main Outcomes
VNS Animal studies					
Meregnani et al. ⁶²	Rats with TNBS-induced colitis	Direct VNS; left cervical VN	5 Hz, 10 sec on, 90 sec off, 500 µs, 1 mA	3 h/d for 5 d	Weight loss and inflammatory indicators were decreased, and the multivariate index of colitis improved.
Sun et al. ⁶³	Rats with TNBS-induced colitis	Direct VNS; left cervical VN	20 Hz, 30 sec on, 5 min off, 500 ms, 0.25 mA	3 h/d for 6 d	DAI, histological scores, MPO activity, iNOS, TNF-, and IL-6 levels all considerably reduced.
Jin et al. ¹¹⁰	Rats with TNBS-induced colitis	Direct VNS; left cervical VN	5 Hz, 10 sec on, 90 sec off, 0.5 ms, 1.0–3.0 mA	3 h/d for 21 d	The autonomic route improved DAI, macroscopic, and microscopic damage.
Meroni et al. ¹¹¹	Mice with oxazolone induced Colitis	Direct VNS; right cervical VN	5 Hz, 1 ms, 1 mA	5 min	The survival rate increased, but colonic and serum cytokines decreased.
Payne et al. ¹¹²	Rats with TNBS-	Direct VNS; the	10 Hz, 30 sec on, 5 min	3 h/d for 5 d	Stool quality and blood were improved, but plasma C-reactive protein and

	induced inflammation of the small intestine	anterior abdominal VN	off, 200 µs, 1.6 mA		inflammatory cell populations in the gut were decreased.
Clinical studies					
Clarencon et al. ¹¹³	1 ileal CD patient (CDAI = 330)	Direct VNS; left cervical VN	10 Hz, 30 sec on, 5 min off, 500 µs, 0.5–1.0 mA	12 mo	At month 12, there was a considerable clinical improvement, a gradual decrease in the CDAI score, and an endoscopic remission.
Bonaz et al. ⁹⁷	7 ileo-colonic CD patients (CDAI 220–450)	Direct VNS; left cervical VN	10 Hz, 30 sec on, 5 min off, 500 µs, 0.25– 1.25 mA	>6 mo	5 patients progressed to clinical, biological, and endoscopic remission, with restored vagal tone.
D’Haens et al. ¹¹⁴	16 biologic refractory CD patients (CDAI 220–450)	Direct VNS; NA of site	NA	1 min QD to 5 min QID for 16 wk	CDAI, faecal calprotectin, and SES-CD levels dropped, as did serum IL-1, TNF-, TNF-, and IFN- levels.

Kibleur et al. ¹¹⁵	9 ileo-colonic CD patients	Direct VNS; left cervical VN	10 Hz, 30 sec on, 5 min off, 500 µs, 0.5–1.25 mA	12 mo	CDAI, faecal calprotectin, anxiety level, and vagal tone were all improved.

Abbreviations: CDAI, Crohn’s Disease Activity Index; DSS, dextran sulfate sodium; iNOS, inducible nitric oxide synthase; MPO, myeloperoxidase; NA, not available; SES-CD, Simple Endoscopic Score for Crohn’s Disease; TNBS, 2,4,6-trinitrobenzenesulfonic acid.