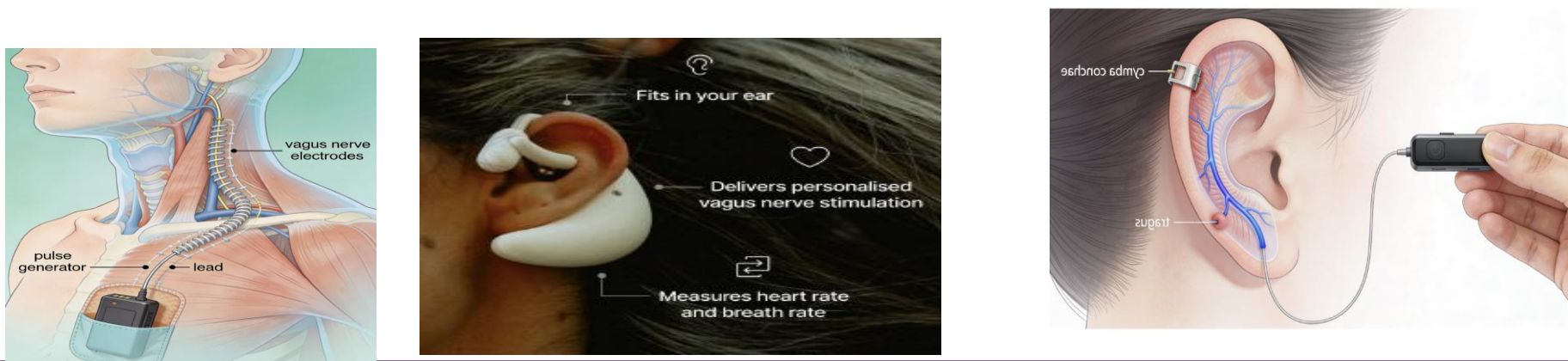


Defining Vagal Nerve Stimulation Protocols for physical and cognitive frailty: review and multistakeholder consensus approach.

P#1600



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Key messages: 9 studies (4 RCTs) show taVNS is safe & feasible in MCI/dementia; cognitive stabilisation is common
Emerging mood/sleep/agitation/anxiety benefits;
Care situations-RCTs needed. Device choices should have CE mark and aim for MHRA regulation

INTRODUCTION	METHODS	RESULTS	RESULTS	CONCLUSIONS																																																																																																																																																								
Vagus nerve stimulation (VNS) is a neuromodulation approach that targets a key conduit between brain and body. VNS can be implanted or trans auricula (TA), and modulates noradrenergic, cholinergic and inflammatory pathways implicated in Alzheimer’s disease and related dementias. The market for direct-to-consumer and healthcare neuromodulation gadgets is booming, fueled by sophisticated marketing and patient desperation. There is clinical use on epilepsy and post stroke. However, evidence on optimal dosing protocols and trial designs remains fragmented. This systematic review synthesises evidence on VNS and taVNS in MCI/dementia/frailty with a dual focus: (1) cognitive and mechanistic outcomes (2) psychosocial, sleep and caregiver-relevant effects, to inform the design of pragmatic care-home trials targeting neuropsychiatric symptoms and sleep within routine dementia care.	PRISMA systematic search across 4 databases (OVID-Embase/PsycINFO, ESCBO-Medline/CINAHL, Web of Science): Filters: (Dementia OR MCI OR cognitive impairment OR frailty NOT epilepsy) AND (taVNS OR VNS OR auricular stimulation) AND (RCT OR cohort OR longitudinal) AND (sleep OR mood OR depression OR anxiety) Screening: 39 FT → Excl: protocols(3), reviews(3), TMS(18), no intervention(15) → 9 studies included.	No study directly compared stimulation parameters to establish dose–response relationships. Stimulation frequencies for taVNS (Transauricular vagus nerve stimulation) ranged from 2–100 Hz, intensities from 0.5–10 mA, and treatment durations between 15-60 minutes, on single sessions or between 4-7 days per week, over a period of two weeks to three months. Five studies measured physical outcomes, and focused on functional/postural performance tasks (6-min walk, TUG, FTSTS, hand-grip dynamometry), exercise endurance, or change in symptomology (e.g., Tremor amplitude). Cognitive assessments varied widely (e.g. MoCA, episodic memory tasks), as did quality of life and mood measures (e.g. SF 36, POMS).	<table><tr><th>Study</th><th>Outcome</th><th>Int</th><th>Ctrl</th><th>Standardised Mean Difference</th><th>SMD</th><th>95% CI</th><th>Weight</th></tr><tr><td>Báez-Suárez 2025</td><td>Sleep Quality</td><td>14</td><td>10</td><td>-0.37</td><td>-0.37</td><td>[-1.19, 0.45]</td><td>10.9%</td></tr><tr><td>Fallgatter 2005</td><td>P1 Latency (C4-F4)</td><td>20</td><td>39</td><td>-0.65</td><td>-0.65</td><td>[-1.41, -0.28]</td><td>11.6%</td></tr><tr><td>Gianlorenpo 2024</td><td>HF-HRV (change score)</td><td>20</td><td>18</td><td>1.90</td><td>1.90</td><td>[1.12, 2.68]</td><td>11.0%</td></tr><tr><td>Laurido-Soto 2025</td><td>Stroke Severity</td><td>17</td><td>18</td><td>0.21</td><td>0.21</td><td>[-0.46, 0.87]</td><td>11.3%</td></tr><tr><td>Shin 2025</td><td>Visuospatial Working Memory Accuracy</td><td>20</td><td>20</td><td>0.29</td><td>0.29</td><td>[-0.33, 0.91]</td><td>11.5%</td></tr><tr><td>Srinivasan 2024</td><td>Anxiety Severity</td><td>21</td><td>21</td><td>-0.32</td><td>-0.32</td><td>[-0.93, 0.29]</td><td>11.5%</td></tr><tr><td>Stavakis 2022</td><td>Global Longitudinal Strain</td><td>24</td><td>24</td><td>-0.98</td><td>-0.98</td><td>[-1.59, -0.38]</td><td>11.5%</td></tr><tr><td>Teruel-Hernández 2023</td><td>Global Cognition</td><td>10</td><td>10</td><td>3.04</td><td>3.04</td><td>[1.68, 4.41]</td><td>9.0%</td></tr><tr><td>Wang 2022</td><td>Global Cognition</td><td>25</td><td>27</td><td>0.61</td><td>0.61</td><td>[0.05, 1.16]</td><td>11.6%</td></tr><tr><td>Random effects model</td><td></td><td>171</td><td>187</td><td>0.32</td><td>0.32</td><td>[-0.47, 1.11]</td><td>100.0%</td></tr><tr><td colspan="8">Heterogeneity: $I^2 = 88.3\%$; $\tau^2 = 1.3115$, $p < 0.0001$</td></tr></table> <table><tr><th>Study</th><th>Outcome</th><th>Int</th><th>Ctrl</th><th>Standardised Mean Difference</th><th>SMD</th><th>95% CI</th><th>Weight</th></tr><tr><td>Wang 2022</td><td>MoCA-B</td><td>25</td><td>27</td><td>0.61</td><td>0.61</td><td>[0.05, 1.16]</td><td>26.3%</td></tr><tr><td>Teruel-Hernández 2023</td><td>MEC de Lobo</td><td>10</td><td>10</td><td>3.04</td><td>3.04</td><td>[1.68, 4.41]</td><td>20.5%</td></tr><tr><td>Shin 2025</td><td>Visuospatial 2-back Accuracy (%)</td><td>20</td><td>20</td><td>0.29</td><td>0.29</td><td>[-0.33, 0.91]</td><td>26.5%</td></tr><tr><td>Laurido-Soto 2025</td><td>NIHSS</td><td>17</td><td>18</td><td>0.21</td><td>0.21</td><td>[-0.46, 0.87]</td><td>26.2%</td></tr><tr><td>Random effects model</td><td></td><td>72</td><td>75</td><td>0.92</td><td>0.92</td><td>[-0.24, 2.07]</td><td>100.0%</td></tr><tr><td colspan="8">Heterogeneity: $I^2 = 79.4\%$; $\tau^2 = 1.2041$, $p = 0.0022$</td></tr></table> Consensus Group 4 PPIE meetings 35 participants Clinicians meeting x12 – identified benefits on non invasive VNS and trial need. Themes: time (dose)- how long each treatment, data collection, concerns about acceptability and side effects (headache/tingling). PPIE rated memory and sleep benefit as most important	Study	Outcome	Int	Ctrl	Standardised Mean Difference	SMD	95% CI	Weight	Báez-Suárez 2025	Sleep Quality	14	10	-0.37	-0.37	[-1.19, 0.45]	10.9%	Fallgatter 2005	P1 Latency (C4-F4)	20	39	-0.65	-0.65	[-1.41, -0.28]	11.6%	Gianlorenpo 2024	HF-HRV (change score)	20	18	1.90	1.90	[1.12, 2.68]	11.0%	Laurido-Soto 2025	Stroke Severity	17	18	0.21	0.21	[-0.46, 0.87]	11.3%	Shin 2025	Visuospatial Working Memory Accuracy	20	20	0.29	0.29	[-0.33, 0.91]	11.5%	Srinivasan 2024	Anxiety Severity	21	21	-0.32	-0.32	[-0.93, 0.29]	11.5%	Stavakis 2022	Global Longitudinal Strain	24	24	-0.98	-0.98	[-1.59, -0.38]	11.5%	Teruel-Hernández 2023	Global Cognition	10	10	3.04	3.04	[1.68, 4.41]	9.0%	Wang 2022	Global Cognition	25	27	0.61	0.61	[0.05, 1.16]	11.6%	Random effects model		171	187	0.32	0.32	[-0.47, 1.11]	100.0%	Heterogeneity: $I^2 = 88.3\%$; $\tau^2 = 1.3115$, $p < 0.0001$								Study	Outcome	Int	Ctrl	Standardised Mean Difference	SMD	95% CI	Weight	Wang 2022	MoCA-B	25	27	0.61	0.61	[0.05, 1.16]	26.3%	Teruel-Hernández 2023	MEC de Lobo	10	10	3.04	3.04	[1.68, 4.41]	20.5%	Shin 2025	Visuospatial 2-back Accuracy (%)	20	20	0.29	0.29	[-0.33, 0.91]	26.5%	Laurido-Soto 2025	NIHSS	17	18	0.21	0.21	[-0.46, 0.87]	26.2%	Random effects model		72	75	0.92	0.92	[-0.24, 2.07]	100.0%	Heterogeneity: $I^2 = 79.4\%$; $\tau^2 = 1.2041$, $p = 0.0022$								Heterogeneous taVNS protocols (2–100 Hz, 0.5–10 mA, variable duration/frequency) preclude clear dose–response inference for cognitive or frailty outcomes. Physical frailty measures were limited and functionally oriented (e.g., TUG, 6MWT, grip strength), with inconsistent evidence across short intervention windows. Cognitive outcomes lacked standardisation, spanning global (MoCA) to domain-specific (episodic memory) measures, reducing comparability and synthesis. Overall, methodological variability and absence of parameter optimisation limit conclusions on taVNS efficacy for cognition–frailty interplay. Clinical academics and PPI strongly supportive CONTACT Christopher.Fox@Exeter.ac.uk Supported by NIHR National Institute for Health and Care Research ALZHEIMER'S ASSOCIATION AAIC Neuroscience Next
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