

1 Aims and hypothesis

To review whether current evidence supports the use of transcutaneous auricular vagus nerve stimulation (taVNS) in people with intellectual disability (ID) and consider the rationale for further study.

The review weighs a **proposition, not an intervention**: that modulating vagal and autonomic pathways could matter for clinically important problems in ID.

2 Background

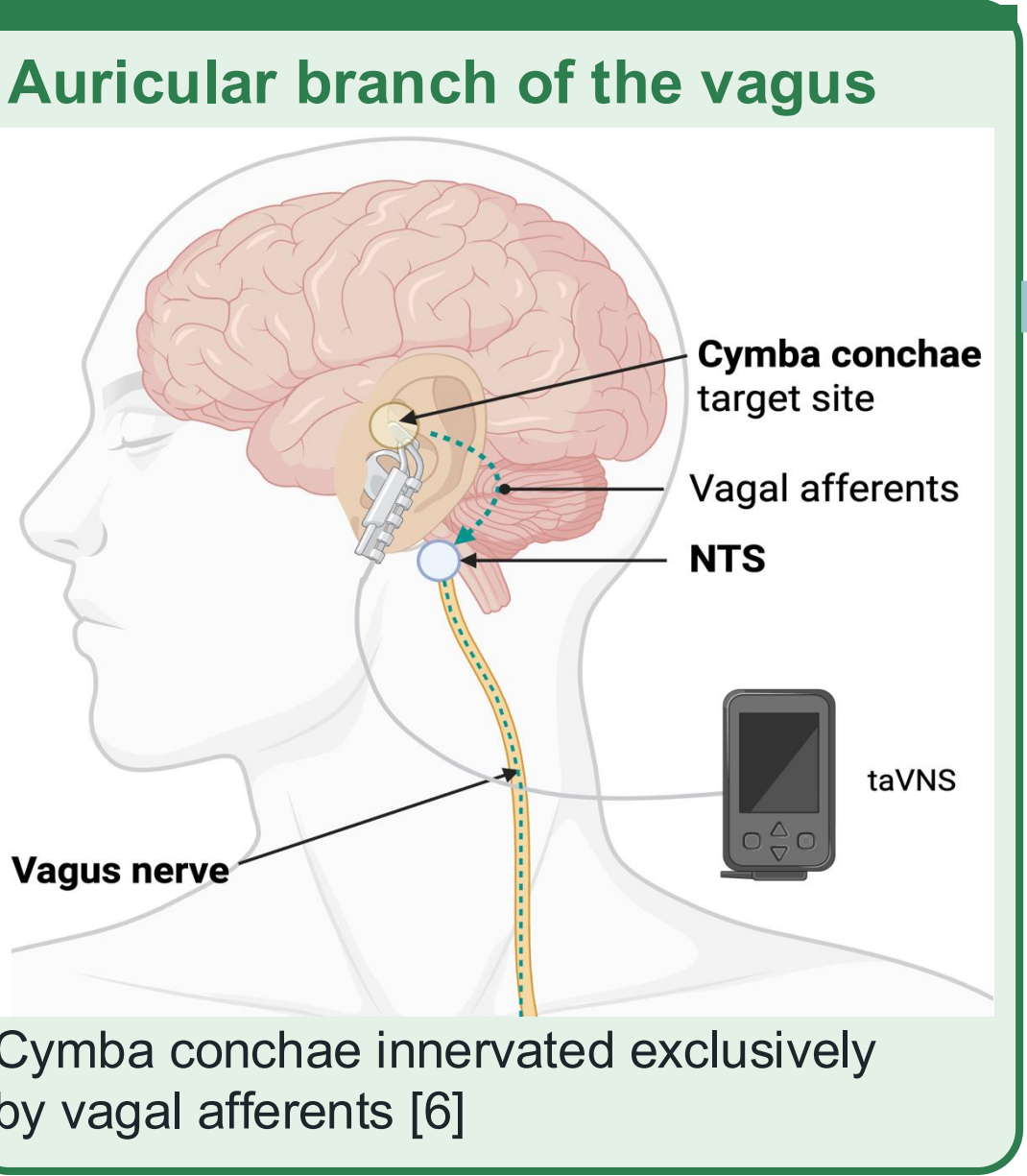
People with ID carry a heavy burden of epilepsy, psychiatric illness, behavioural dysregulation and sleep disturbance, often managed symptomatically by numerous interventions and polypharmacy [1,2]. They are often excluded from trials of mechanism-based treatments [3,4].

taVNS is a non-invasive method of stimulating vagal afferents at the ear, proposed as a low-burden way to influence the brain-body pathways involved in these psychiatric, behavioural and autonomic disturbances [5,9].

3 Methods

A narrative review critically examining the evidence base on taVNS and vagal nerve stimulation. It covers vagal mechanisms and human target engagement, implanted VNS in epilepsy (including ID cohorts), taVNS in epilepsy and other neuropsychiatric populations, autism and ID-relevant genetic syndromes, behaviour that challenges and safety and feasibility. At each step, the review asks how far findings from populations without ID extrapolate to people with ID.

4 Why the vagus? A mechanistic chain, graded link by link



Nucleus tractus solitarius (NTS)
Engaged in humans: fMRI activation of NTS with cymba-conchae, not earlobe, stimulation [6,7]

Locus coeruleus · raphe · parabrachial · hypothalamus
Noradrenergic and serotonergic relay: LC/raphe fMRI response; pupil dilation and alpha attenuation [6,8]

Arousal/ affect/ autonomic balance/ plasticity/ neuroimmune tone
Characterised mostly in animals; human evidence rests on indirect markers and small effects [9,22]

Outcomes that matter in ID
Seizures, sleep, emotional and behavioural dysregulation, learning readiness - no direct data

Autonomic dysregulation is consistently reported across ID-associated syndromes, supporting the vagus nerve as a mechanistically plausible target and providing a rationale for phenotype-selected trial design.

Rett syndrome
Sympathetic predominance, vagal withdrawal, prolonged QTc; raised sudden-death risk [10,37]

Down syndrome
Reduced RMSSD on meta-analysis of 13 studies; blunted autonomic reactivity to challenge [11]

Fragile X syndrome
Autonomic hyperarousal in 86% of studies finding a group difference (2026 systematic review) [12]

Autism
Lower parasympathetic HRV ($g \approx -0.52$, 34 studies) [13]; SUDEP $\approx 3\times$ general population in ID [3]

5 Results: the evidence is inferential, not direct

Each tier is one analogical step further from the target question. Directness decreases downward; the target itself - efficacy in ID - is an evidence void.

Implanted VNS in drug-resistant epilepsy - including ID cohorts	Guideline-endorsed; roughly half achieve $\geq 50\%$ seizure reduction. In developmental and epileptic encephalopathies seizures fell 42%, alertness improved in 63% vs 32% without ID. Caveat: a paediatric meta-analysis found lower seizure response when ID is present [14,15,16,17]
taVNS in epilepsy	Four sham-controlled RCTs ($n = 368$): seizure frequency reduced, responder rate not significantly different. A double-blind study in refractory temporal lobe epilepsy improved working-memory reaction time, though not accuracy. Paediatric pilot ($n = 14$): 54% seizure reduction, no severe adverse events [18,19,20]
taVNS in autism and other neuropsychiatric populations	An at-home, caregiver-administered study in autistic children (88.5% session completion) supports a possible delivery model, but required $IQ \geq 70$ and did not include participants with ID. Cognitive effects elsewhere are small, mood effects rest on low-certainty trials [21,22,23]
ID-relevant genetic syndromes - the closest signal	Prader-Willi syndrome (PWS) (adults with ID; $n = 5$, non-blind): daily t-VNS reduced temper outbursts in 4 of 5 after 9 months, worsening when dose was halved; taVNS raised circadian vagal HRV and higher HRV predicted fewer outbursts. Fragile X mouse: memory persistence improved. No sham-controlled human data. [24,25,26]
Controlled efficacy of taVNS in people with ID	<i>No sham-controlled efficacy data. Beyond epilepsy there is weak evidence to suggest that taVNS improves outcomes in people with ID</i>

$\approx 50\%$	of people with drug-resistant epilepsy achieve $\geq 50\%$ seizure reduction with implanted VNS [14,15]
63%	of people with developmental and epileptic encephalopathies had improved alertness on VNS (vs 32% without ID) [16]
6,322	participants across 177 taVNS studies: no difference in adverse-event risk versus control [27]
$IQ \geq 70$	entry criterion of the home-delivered autism study most often cited as feasibility evidence for ID [21]
0	sham-controlled trials of taVNS conducted in people with ID

6 Does the case extend to behaviour that challenges?

The problem Aggression, self-injury and emotional outbursts are common in ID and drive placement breakdown and antipsychotic use. In 82 RCTs, every intervention yields only small effects ($SMD \approx -0.4$). A mechanism-based adjunct would have clear value. [2,28]	Arousal precedes the behaviour Heart rate rises 22% a minute before challenging behaviour in autistic children (AUC 0.72); wearables predict aggression 3 minutes ahead (AUROC 0.80, 43% with ID); vagal HRV (RMSSD) falls before high-tension states in adults with ID. [29,30,31]	A direct vagal signal Implanted VNS improved maladaptive behaviour in PWS: taVNS reduced temper outbursts in 4 of 5 adults dose-dependently, with raised 24-hr vagal tone and higher HRV predicting fewer outbursts. In epilepsy, VNS improves behaviour and mood independently of seizure control [24-5,32-3]	What follows Behaviour that challenges is a defensible primary endpoint, for a taVNS trial in ID: carer-rated irritability and outburst counts, with ambulatory HRV as the engagement marker. An adjunct to positive behaviour support.
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7 Why this population? The burden that motivates a vagal target

	What the evidence shows	Why it motivates a vagal
Epilepsy	Over-represented and often refractory. SUDEP $\approx 3\times$ risk [1,3]	Seizure networks are modifiable by vagal stimulation
Psychiatric and behavioural	High rates of anxiety, mood symptoms and behaviour that challenges [1,2]	Arousal and affect regulation are candidate targets
Sleep	Common, multifactorial - worsens behaviour, cognition and seizure threshold [9]	Arousal and affect regulation are candidate targets
Autonomic function	Dysregulated stress reactivity, arousal, GI function and possibly seizure susceptibility in a subset [9,10]	Direct, mechanistically motivated rationale
Polypharmacy	Common and rising in people with ID [2]	A low-burden adjunct that reduced medication load
Care and access	Treatment delivery depends on family or paid carers; the population is routinely excluded from intervention trials [4,21]	Non-invasive, home-deliverable interventions are deliverable

8 Safety and implementation

	Key safety findings	ID-relevant caveat
Kim 2022 · systematic review & meta-analysis [27]	177 studies, 6,322 participants- no difference in AE risk versus control; no link to severe events. Mostly ear pain, headache, tingling	More than half of studies did not report AEs at all. Samples largely excluded ID
Gerges 2024 · scoping review [5]	21 clinical populations- AEs mostly local; no consistent serious-harm signal	Parameter reporting inconsistent, sham frequently weak
Giraudier 2025 · pooled analysis ($n = 488$) [35]	SEs minimal and mild. Interval stimulation produced fewer side effects than continuous	Young adults who are not sensory-sensitive or carer-dependent
Black 2023 · home pilot in autism [21]	22 mild AEs; carer-delivered, remotely supervised home use feasible; no serious events	$IQ \geq 70$ - does not establish tolerability in ID
Implanted VNS [14,34]	Hoarseness, cough, higher infection risk in children; serious SEs rare	Non-invasive taVNS avoids these

9 Critical appraisal of the evidence base

Study Quality Mostly small, open-label or single-arm studies (e.g. Prader-Willi, $n = 5$, non-blind) and indirect surrogate markers (HRV, fMRI) rather than direct clinical outcomes. No sham-controlled taVNS trial in ID.	Patient and carer perspectives Only the Prader-Willi study formally assessed carer and patient acceptability: outbursts shortened, 4 of 5 participants exceeded carer-set goals, compliance exceeded 86%, and all completers chose to continue t-VNS [24]. Elsewhere, only completion rates and adverse events were captured.	High-income vs Low- and Medium-income settings No study identified involves a low- or lower-middle-income populations or the feasibility of taVNS delivery in these settings
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10 Conclusions

The current case for taVNS in ID is one for **research, not yet treatment**

This current evidence base justifies studying taVNS directly in ID, to establish efficacy, acceptability and feasibility, in staged, phenotype-selected, sham-controlled trials built around carer-relevant outcomes

References

Full reference list available upon request from authors: prashanth.desilva@psych.ox.ac.uk