Do Motor Skills Predict Response to Neuromodulation-Paired Feeding in At-Risk Infants?

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Introduction

- Feeding readiness in infants is supported by early motor control, postural stability, and emerging neurophysiological integration. Delays in these areas often prolong the transition to full per oral (PO) feeds and increase the likelihood of gastrostomy (G-tube) placement.
- **Transcutaneous auricular vagus nerve stimulation (taVNS)** has emerged as a novel neuromodulation strategy to enhance neuroplasticity and support feeding skill acquisition. The BabySTrong system, developed at Medical University of South Carolina (MUSC), pairs brief taVNS electrical pulses with bottle feeding.[1]

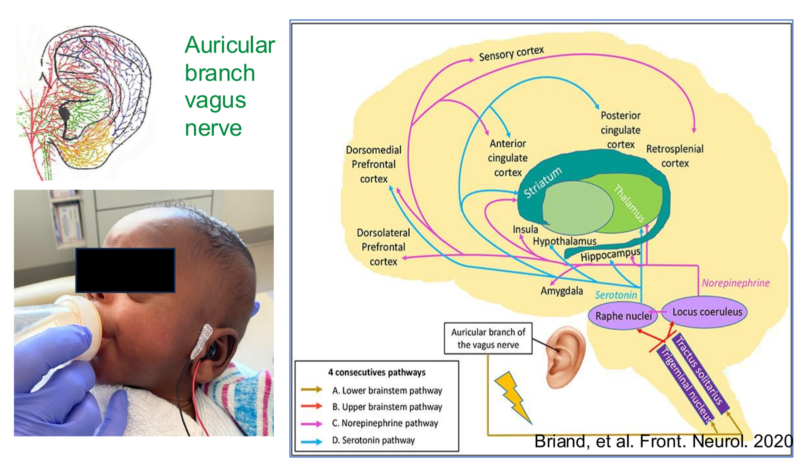

Figure 1. Transcutaneous microcurrent stimulation at auricular vagus n. (green area) transmits to dorsal motor nucleus and locus coeruleus, thalamus, cortex. **taVNS boosts active circuits via release of norepinephrine, serotonin and acetylcholine, and has multiple effects on neuroinflammation.**[2]

- Data from prior pilot trials suggests that pairing feeding with taVNS may affect specific head and neck movements, to a greater extent, in infants who are able to attain full oral feed.[3]
- taVNS paired with CIMT may improve upper-limb function in infants.[4]
- taVNS paired with active motor practice, has also been shown to improve upper-limb function in adults following stroke, demonstrating its capacity to enhance activity-dependent neuroplasticity.[5-6]
- **These positive results support the need to further investigate the effect of taVNS on the early motor movements of at-risk infants.**

Project Description

- This project includes retrospective secondary analysis of data previously collected during the BabyStrong I trial, conducted at MUSC.
- Data from the BabyStrong I trial were made available for educational and scholarly analysis.
- This data analysis is paired with a clinical implementation project to create updated training videos for the **Specific Test of Early Infant Motor Performance (STEP)**[7-8] for NICU clinicians and BabyStrong II partners; which include the Children's Wisconsin and University of Wisconsin-Madison.
- The **project aligns with HPU's core values** through the responsible, and ethical use of existing research data, the creation of supportive clinical training resources, and collaboration across multiple professions and institutions.

Purpose/Aims

1. To determine whether pre-treatment STEP scores predict feeding treatment response in infants receiving taVNS-paired feeding intervention, where "Responder" is defined as achieving full oral feeds.
2. To examine whether taVNS-paired feeding contributes to motor skill changes in high-risk infants, and whether these changes differ in Responders and Non-Responders.

References

BabySTrong taVNS-Paired Bottle Feeding to Improve Oral Feeding (1R41HD104409)

Methods

Study design: Retrospective secondary analysis of data collected during the BabySTrong phase I trial under IRB-approved study protocol

Data Analysis Approach: Modeling of STEP trajectories; logistic regression with modeling to predict response to treatment; rate-of-change analyses; repeated-measures across intervals, descriptive statistics

BabySTrong Phase I design: 17 term-equivalent aged (TEA) infants consulted for G-tube (1 withdrawal); randomized, controlled, double-blinded (Participant, Outcomes Assessor), crossover feasibility and safety study; parental consent. *NCT04849507*. Infants randomized to Active taVNS (delivered current during feed) and Sham taVNS (no delivered current during feed); 1 withdrawal prior to treatment.

taVNS treatment: Electronic pulse generator units (Soterix) delivered microcurrent pulses via tragus of left ear electrode (25Hz, pulse width 500μsec), 'on' with suck 'off' with rest, at 0.1mA< perceptual threshold.[1]

Treatment groups: **Intervention Frequency and Duration:** 10-day primary phase consisting of twice-daily (2x/day) taVNS-paired feeding sessions; up to 17 days total of taVNS-paired feedings depending on crossover status; **Crossover component:** If infants failed to make progress after the first 10 days (<4ml/kg/day) they would be crossed over to the opposite treatment group (Active <-> Sham) for up to an additional 7 days.

Results/Outcomes

Table 1. Demographics of Infants		Baby Strong 1 Subjects (N=16)	Responders (Full PO) (N=8)	Non-Responders (G-tube) (N=8)	p-value
Birth information					
Sex	Male	8	3	5	0.62
	Female	8	5	3	
Birth weight (grams)		1350.75 ± 924.6	1126.63 ± 891.69	1574.88 ± 960.2	0.35
GA at Birth (weeks)		28.87 ± 5.29	26.95 ± 5.32	30.79 ± 4.83	0.15
GA at Enrollment (weeks)		43.5 ± 4.12	42.14 ± 1.89	44.86 ± 5.35	0.21
Medical History					
GERD		12	4	8	0.077
Chorio		2	1	1	1
IVH		4	Grade I [2]	Grade 1 [1] Grade 4 [1]	1
taVNS information (Mean ± SD)					
# days attempting PO until taVNS start		34.31 ± 15.68	37.63 ± 16.93	31 ± 14.67	0.42
Total number of taVNS sessions		27.93 ± 7.64	26.25 ± 9.51	29.63 ± 5.29	0.4
STEP information (Mean ± SD)					
STEP score pre-TX		16.75 ± 3.97	19 ± 2.33	14.5 ± 4.12	0.021
STEP score Day 10		18.94 ± 4.92	19.63 ± 4.47	18.25 ± 5.59	0.59
STEP score d/c (after crossovers)		19.44 ± 4.38	19.5 ± 5.04	19.38 ± 3.96	0.96

Note: GA = gestational age; Chorio = chorioamnionitis; IVH = intraventricular hemorrhage

- No significant differences between Responder and Non-Responder groups except for Pre-Treatment STEP scores and incidence of GERD (Table 1)
- Infants who achieved full oral feeds (**Responders**) entered treatment with **significantly higher Pre-Treatment STEP scores** than Non-Responders (p = .017).
- **Higher early STEP scores increased the odds of treatment response** (OR = 1.60, 95% CI [1.10, 3.01], p = .053).

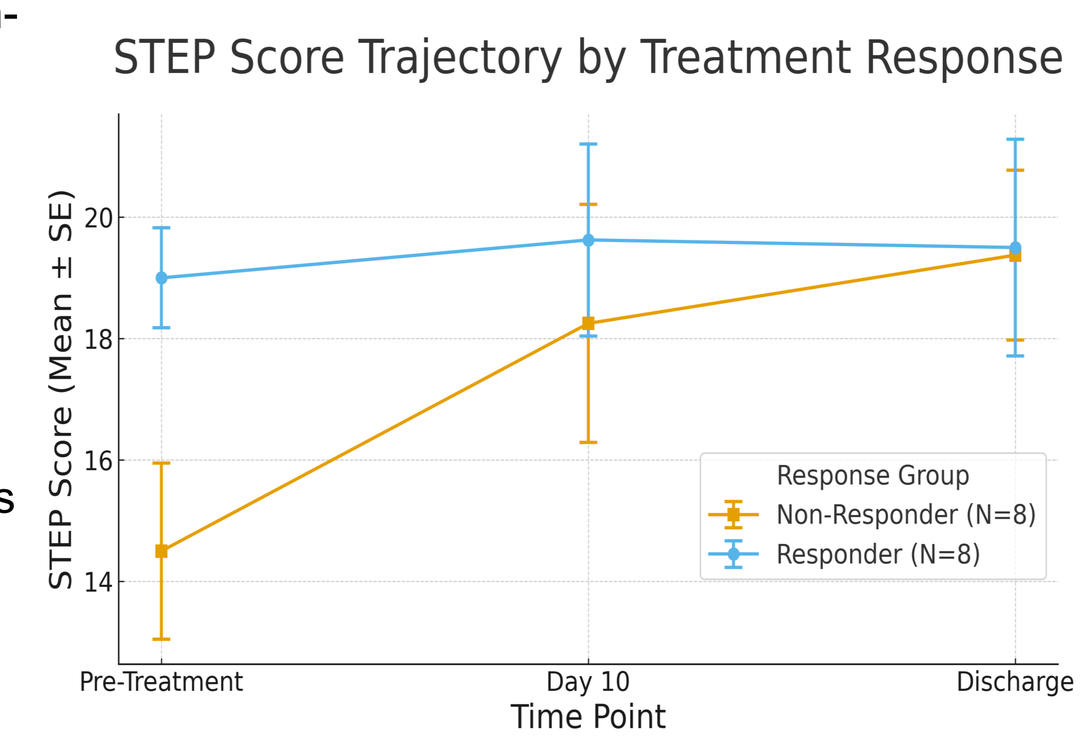

Figure 2. Line Plot of STEP Scores by Response Group. Non-Responders demonstrated significant within-group improvement from Pre-Treatment to Discharge (mean change = 4.88 points; p = .018), whereas Responders had above cut-off STEP scores (16 points) at study start and showed minimal change (0.5 points).

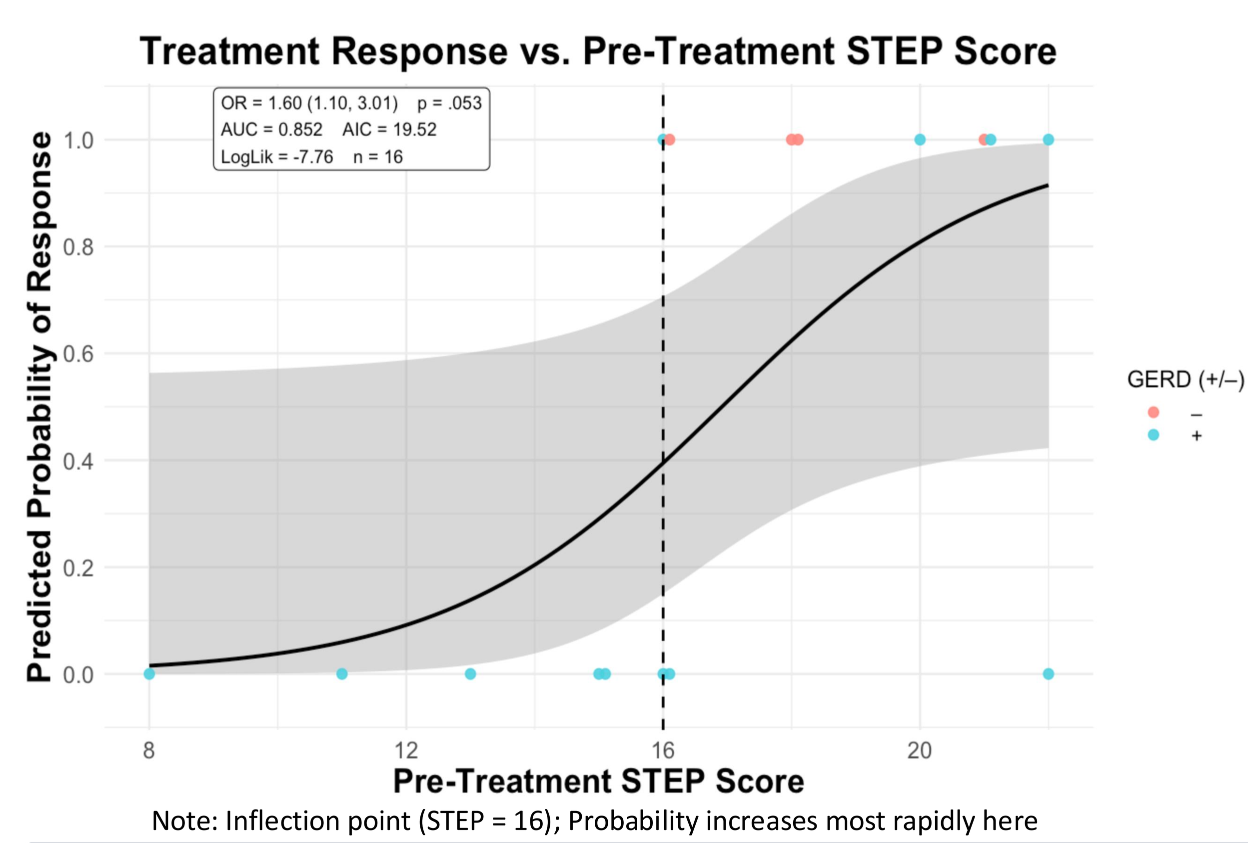

Figure 3. Logistic Regression of Response Status Predicted by Pre-Treatment STEP Score including presence of GERD. S-curve illustrating the predicted probability of being classified as a Responder as a function of Pre-Treatment STEP score. GERD-positive infants, particularly Non-Responders, clustered in the lower predicted-probability range.

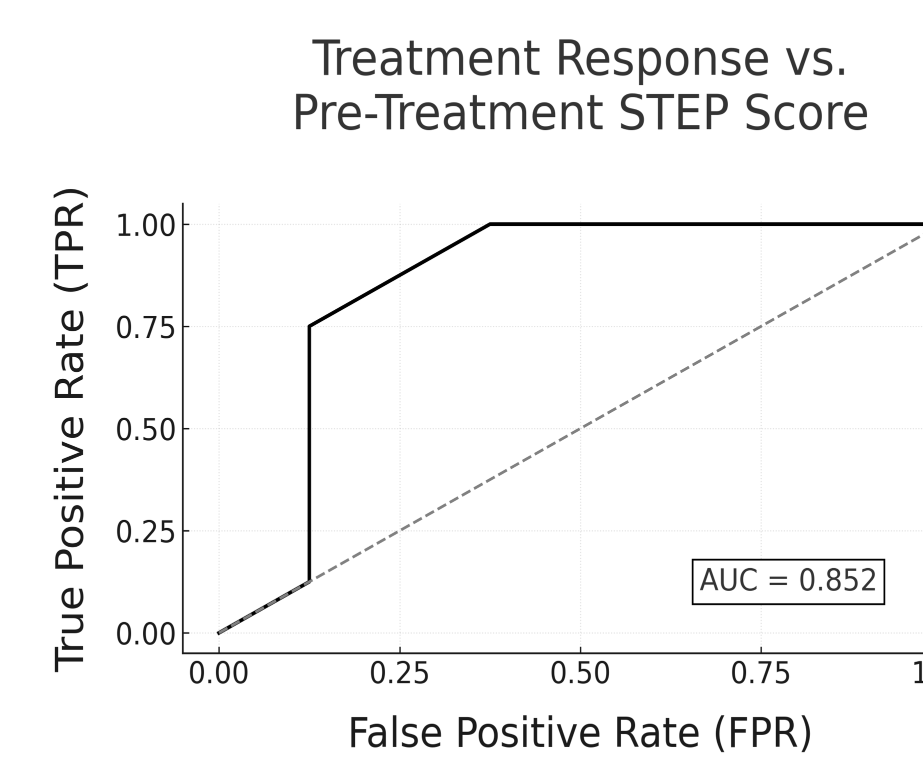

Figure 4. Receiver operating characteristic (ROC) curve of logistic regression. ROC curve showing strong discrimination (AUC = 0.852) for Pre-Treatment STEP scores predicting feeding treatment response (full PO feeds).

Discussion

Clinical Implications:

- Data in this group of TEA infants with feeding failure reinforces STEP cutoff scores to define high vs low risk infants.
- STEP scores indicate that early motor skills may have a prognostic value in determining success with a taVNS feeding trial for at-risk infants.
- This suggests that STEP values reflect brain injury and motor function essential to early oral feeding.
- However, Non-Responders showed significant improvement in STEP scores despite not achieving full PO feeds. This may reflect progress attributed to taVNS-paired feeding protocol.
- The STEP is brief, noninvasive, and feasible to complete in nursery settings which may help identify infants at risk for prolonged feeding challenges, guide targeted early intervention strategies and engage families in informed discussions about expected developmental trajectories.

Limitations:

- Small pilot sample size, inadequate statistical power to determine a difference between active and sham treatment.

Next Steps:

- This data will impact BabySTrong Phase II trial statistical plan. We will control for pre-treatment STEP scores as a covariate in outcomes assessments.
- Improve interrater reliability across BabySTrong trial II sites through updated BabySTrong training video and handout materials.