

Impact of Vagus Nerve Stimulation on Cognitive and Motor Skills in Rett Syndrome: A Controlled Trial

Hui-Min Chen; Yang-Yang Wang; Xiao-Li Li; Li-Ping Zou

Department of Paediatrics, First Medical Centre, Chinese PLA General Hospital, Beijing 100853, China; State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, Beijing, China

- The VNS group showed developmental improvements compared to the control group, with a medium-to-strong effect size (Cliff's delta = 0.476) despite a non-significant p-value (0.1245).
- Improvements were observed in behavior, social interaction, attention, and slight improvements in hand use and ambulation.
- EEG wavelet entropy differences were notable at week 14 in the treatment group.
- Exploratory endpoints at 26 weeks indicated significant symptom improvements in emotion, attention, and social interaction.

OBJECTIVES

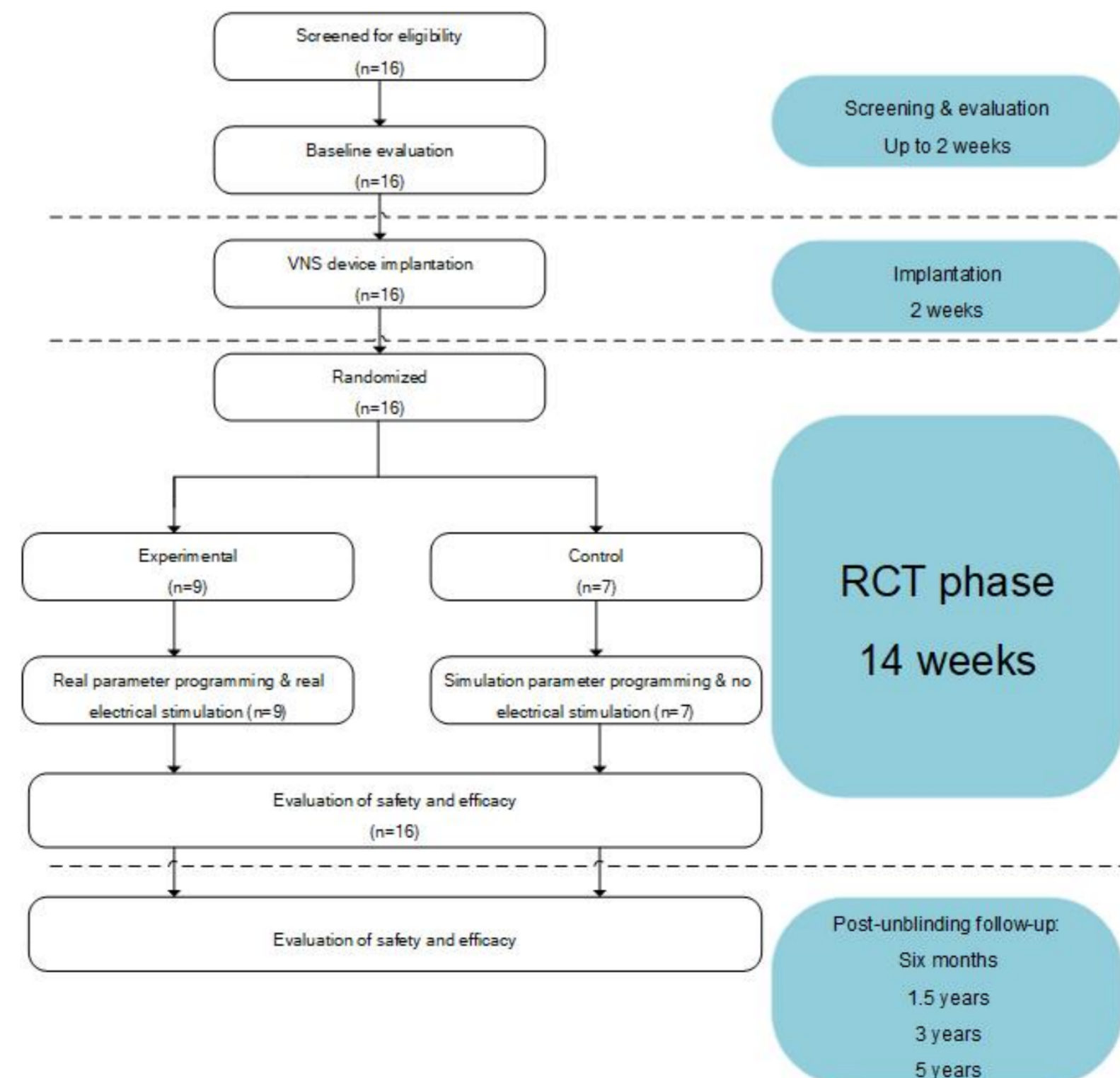
Our research aims to investigate the efficacy of VNS in improving cognitive and motor development in children with Rett syndrome, potentially offering new therapeutic strategies in a field where effective treatments are desperately needed.



Study design

This is a single-centre, randomised, sham-controlled study involving 16 children with Rett syndrome aged 2-7 years who met the 2010 Diagnostic Criteria for Rett syndrome.

The Pinci G112 paediatric VNS device, developed by Tsinghua University and featuring a 14G specification with a National Instrument Registration Certificate number 20163210989, was used. The VNS system consists of a single needle wire (incorporating two stimulation electrodes and a fixed electrode), a pulse generator, an external parameter programming controller, and a magnet. Following a two-week postoperative observation period, a designated safety officer programmed the external parameters. The programmable parameters included pulse amplitude, pulse width, pulse frequency, stimulation duration, and interval time. Programming time points were established at 2, 8, 14, 20, and 26 weeks after surgery.

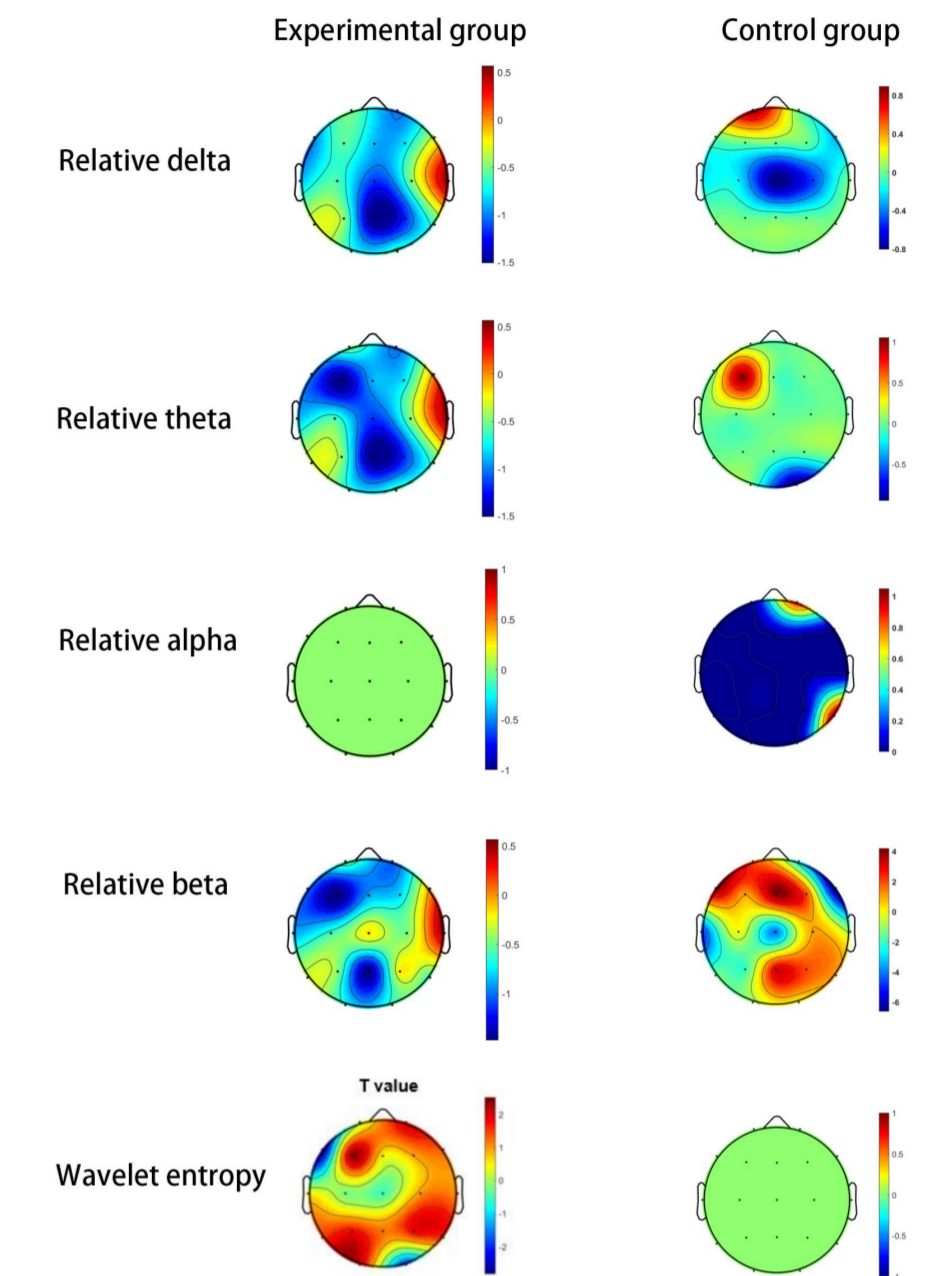
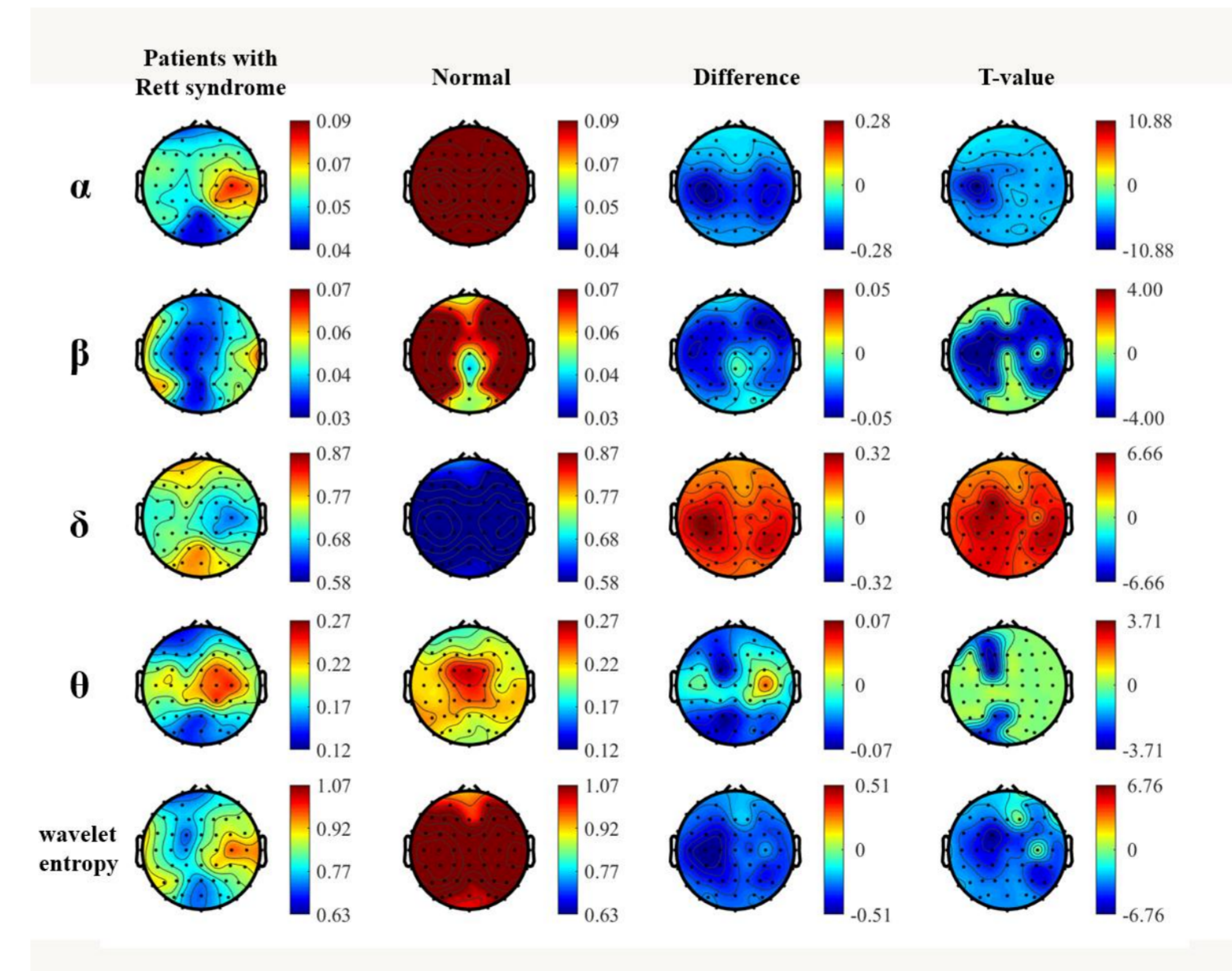


RESULTS OF LORUM IPSEUM

Symptom improvement in patients at week 14 after treatment

	Experimental Group	Control Group	95%CI	p value	Cliff's D
Primary outcome					
Hand use	80(65, 96)	93(78, 95)	(-16,1)	0.1835	-0.41
Ambulation	76(0, 100)	90(50, 100)	(-41,5)	0.1666	-0.42
Seizure	0(0, 25)	0(0,10)	(-3,9)	0.6974	-0.095
Autonomic features	20(0,20)	20(0,32)	(-12,10)	0.6190	-0.15
Behaviour	75(55,95)	90(71,93)	(-21,0)	0.1110	-0.49
Attentiveness	76(60,90)	85(80,90)	(-14,0)	0.1494	-0.44
Social interaction	75(60,90)	88(70,95)	(-16,1)	0.1240	-0.47
Language/communication	90(78,100)	95(70,97)	(-9,7)	0.3295	-0.30
RTT-DSC-VAS	487(363-571)	538(450-600)	(-105,2)	0.1245	-0.47
Secondary outcomes					
Development score	12(9-33)	15(7-28)	(-9,6)	0.7104	-0.12

Differences in EEG Between Patients with Rett Syndrome and Healthy Age-Matched Peers



Differences in EEGs at 14 Weeks Between the Experimental and Control Groups

CONCLUSIONS OF LORUM UPSEUM

In conclusion, our study presents VNS as a promising intervention for addressing the neurodevelopmental challenges in Rett syndrome patients. Further research is needed to confirm these findings and to explore the mechanisms behind the observed improvements, with the goal of enhancing the overall management and quality of life for these patients.

REFERENCES

Adcock KS, Chandler C, Buell EP, et al. Vagus nerve stimulation paired with tones restores auditory processing in a rat model of Rett syndrome. *Brain Stimul.* Nov-Dec 2020;13(6):1494-1503. doi:10.1016/j.brs.2020.08.006

Buchanan CB, Stallworth JL, Scott AE, et al. Behavioral profiles in Rett syndrome: data from the natural history study. *Brain and Development.* 2019;41(2):123-134.

Hays SA. Enhancing Rehabilitative Therapies with Vagus Nerve Stimulation. *Neurotherapeutics: the journal of the American Society for Experimental NeuroTherapeutics.* Apr 2016;13(2):382-94. doi:10.1007/s13311-015-0417-z