Noninvasive spinal neuromodulation and subject-specific rehabilitation of child with cerebral palsy (CP) triggers multiple system neural networks that reorganizes and enhances multiple sensory-motor behaviors

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INTRODUCTION

A child born prematurely with a diagnosis with cerebral spastic diplegia could transform his dysfunctional motor recruitment patterns using a combination of Transcutaneous Spinal Neuromodulation (TSN), combined with a specific activity-training program utilizing alignment of the center of mass, to maximize proprioceptive input to transform the networks into relatively normal functional states. This did occur over a 2-year period and all stimulation was discontinued. Despite follow-up physical therapy treatment, he began return to a more dysfunctional diplegic pattern with decreased activity, which necessitated re-implementation of TSN. The highest motor skill level in CP is that usually that of a typically developing 5-year old child.

METHODS

The 17-year old male subject began a targeted treatment began at age of 19 months, where his Gross Motor Functional Classification Scale (GMFCS) improved from Level 2 to Level 1 following serial casting at age 3 combined with FES to improve ankle range of motion for improved motor skills. At age 12, consistent daily TSN (20 Hz 100 pulse duration and intensity of 18 to 3 mA, depending on activity) was initiated in combination with play activities consistent with his age and interests for 2.5 years. TSN was gradually decreased over time to a schedule of use for only 5 minutes every 3-4 days before it was was discontinued at age 15 for a 17 month period. TSN was reintroduced with EMG data collection occurring the day before implementation (without TSN), and then tested the next day (with TSN). All previous training from age 1-17, and the data collection for reintroduction of TSN were done arms/hands free.

EMG was recorded during the tests with wireless DataLITE Explore system by Biometrics Ltd.

TSN was conducted using Chattanooga Continuum stimulator. Biphasic waveform at 14Hz (patient preference) with a pulse width of 100 µs. Stimulation was applied using two pairs adhesive electrodes (2”x2”) covering the C6(cathode) and T1 (anode) laterally on either side of the spinal columns. Similarly on two pairs of electrodes were attached covering T10 and L1. The stimulation intensity was at 0.5 mA modulated by patient.

Treadmill stepping: the subject stepped on the treadmill at speed of 1,2,3,4,5,6 mph without and with TSN. He was only able to step at 7 mph with TSN.

Jump test: Instructed to jump as high as possible for 5 times.

Sit to Stand: Instructed to maintain sitting position as still as possible for 2 minutes then sit to stand for 5 times.

Standing: Instructed to first standing with both feet placed hip width apart barefooted as till as possible for 90 sec then standing with only one foot for 90 sec.

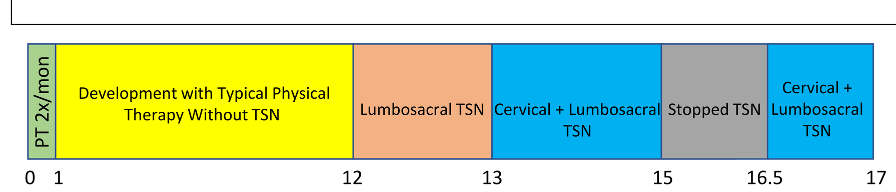

Fig 1. Timeline of the study.

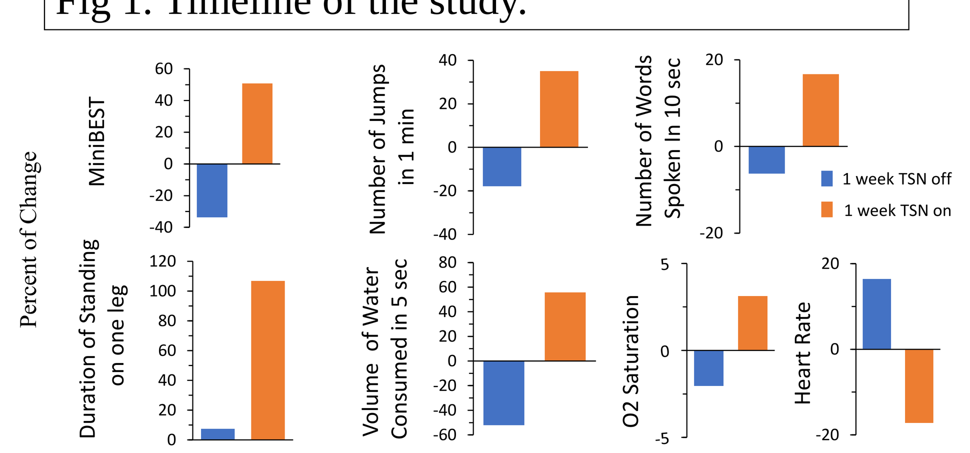

Fig 2. Percent of change in functional and performance parameters after 1 week of TSN off followed by 1 week of 3-6 hr/day of TSN on. This test was done at age of 14.

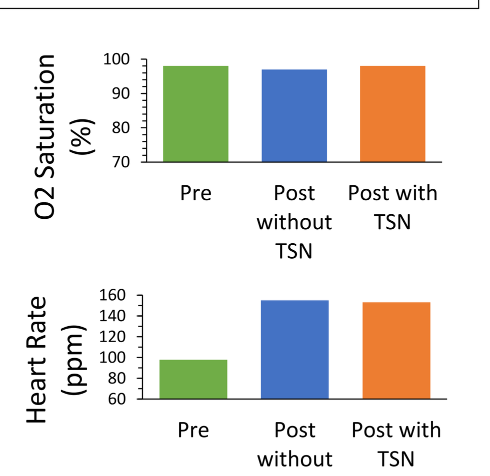

Fig 3. Endurance walking (6mph) on treadmill (1 min) pre TSN and after 8 months of chronic TSN. This test was done at age of 13.

RESULTS

Table1. Selected, but representative Sensory-Motor Skills that Evolved during Development *

Function	Age 12	Age 13	Age 14	Age 15	Age 16	Age 17
Gross Motor	Consistently walked in a more normal gait pattern	Acquired sensation falling backwards on the trampoline	Sit with pelvis upright without stimulation	Demonstrated facial expressions that matched his feelings and state of mind (e.g. motor-eyebrows, being surprised)	Maturity of sensory-motor sensations enabling wearing of a heavy backpack without it interfering with his gait pattern.	Twirling rings consecutively translating the ring on each finger (1-4) and back again (4-1)(after starting TSN again
	Immediately could balance on one leg in standing tree pose with stimulation on	Balance improved-could lie down on his back on horse without falling off	Bounce on ball with arms overhead or twirling hula hoops while bouncing	Could yo-yo using either hand while standing on upside down BOSU ball		
	Improved alignment of all body segments for all gross motor activities	Catch a small ball for the first time	Balanced water bottle on his head when sitting on a stable surface	Performed forward flip on trampoline, landed on feet without losing balance		
		Lost fear of being on the edge of a high surface without falling	Jump rope at 103 times in minute without stopping, and without fatigue. Jumped up on a 20-inch block	Started learning to jump his horse in horse-riding competition		
		Spontaneously demonstrated forwards, backwards and sideward stepping and skipping on treadmill without loss of balance or using arms without ever having practiced	Jumped forward from a 24-inch block	10 repetitions of spinning around on toes of one foot		
		Walked and twirled hula hoops on his arms and even fingers simultaneously	Climbed a 6-foot fence and jumped down on the other side			
			Crawl 10 feet forward and backwards while maintaining balance on the large treatment ball			
			Easily stepping over knee high objects			
Fine Motor Skills		Audible snap better, with L (dominant) hand, R inconsistent		Handwriting spontaneously emerged on non-dominant hand	Obtained driver’s license on first try	Typing all assignments
		2-handed typing spontaneously emerged		Acquired ability to cut using scissors with either hand		Writes equally well with both hands -ambidextrous
				Cut a penny in half using utility scissors using R hand		Rapidly and audibly snaps each finger (1-4) using either hand
				Quit wearing glasses as vision improved (peripheral, 2D to 3D, could judge distances for first time		
				Could feel textures with his fingertips-tactile		
				Could feel the breeze on his face for first time-tactile		
SENSORY (swallowing, vision, hearing, speech)		Reported visual images becoming sharper and colors more vivid and greater depth perception immediately when stimulation was initiated	Could say “s” without a lisp-speech more clear	Became aware of drinking water by swallowing without just pouring down his throat to his stomach	Started filtering out sounds that were unimportant	R side of throat/neck started contracting with swallowing
				Hearing directionality appeared (previously had no awareness of where a sound came from).		Eyes tearing when making a sad face
				Quit headbanging daily as had done since he was an infant		Grades and test scores all excellent
				Reported sleeping continuously throughout the night on a regular basis		Student council officer throughout school
						Photographer for yearbook
						No one in high school knows he has CP

*The behaviors, motor skills and sensory-related events listed in this table are considered to be highly unlikely to have occurred without the combination of TSN and subject-specific activity–dependent guidance of neural network reorganization. This assessment is based on numerous published documents that have documented levels of functions based on the classification of the severity of the developmental dysfunctions and the age of the subject.

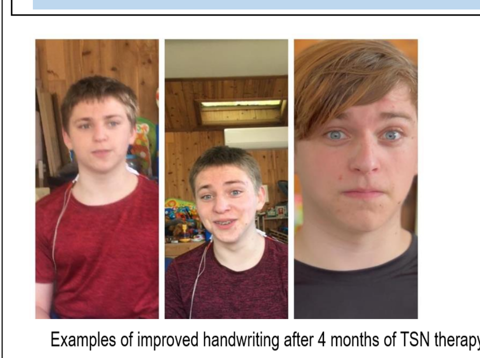

Fig 4. Example of “sad” facial expression changes over a 2-year period using TSN and targeted treatment. All 3 pictures are of him, using maximum effort, to reflect a ”sad” face. There are continued changes in all sensory motor system including vision, hearing, vestibular, swallowing and all fine motor.

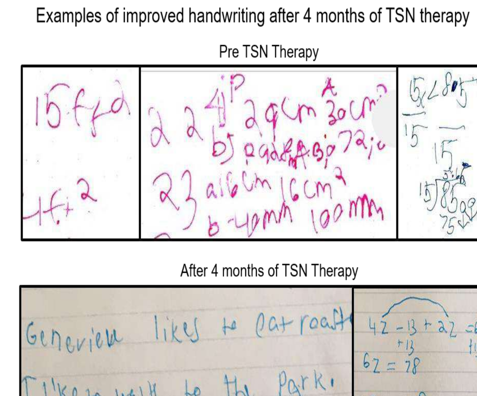

Fig 5. Patterns of handwriting during routine school work before(top) and after (bottom) 4 month of TSN therapy. He now is ambidextrous. His typing speed is 56 words per min with 98% accuracy.

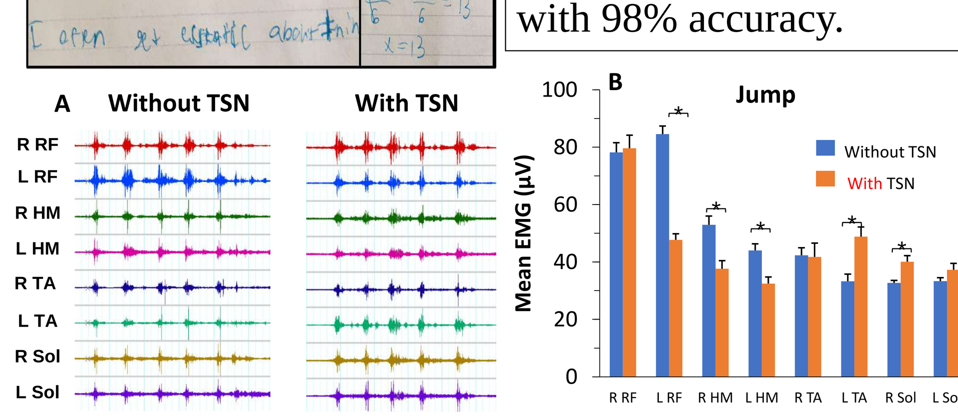

Fig 6. Raw (A) and Mean (B) EMG of five jumps without (blue) and with(orange) TSN. * significant difference. Note that in three of four of the more proximal muscles the mean EMG was significantly lower during the jump whereas for the more distal muscles the left TA and right soleus were significantly higher with TSN. These data suggest that the functional connectivity of the neural networks driving different muscle can be very heterogeneous and asymmetric as a result of CP and\or neuromodulation.

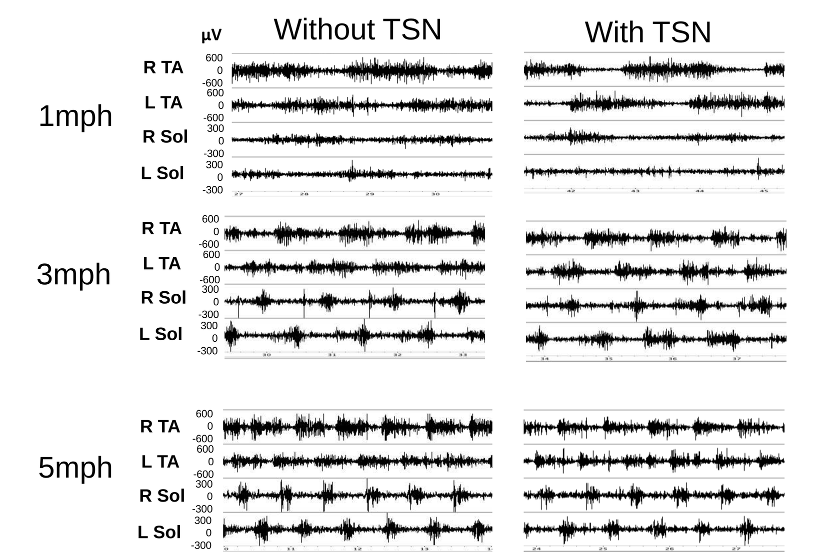

Fig 7. Representative examples of 5 seconds raw EMG of tibialis anterior (TA) and soleus (Sol) muscles while walking on treadmill without and with TSN 24 hours apart. The subject had been without TSN for 17 Months . Quantitative analysis are shown in following figures.

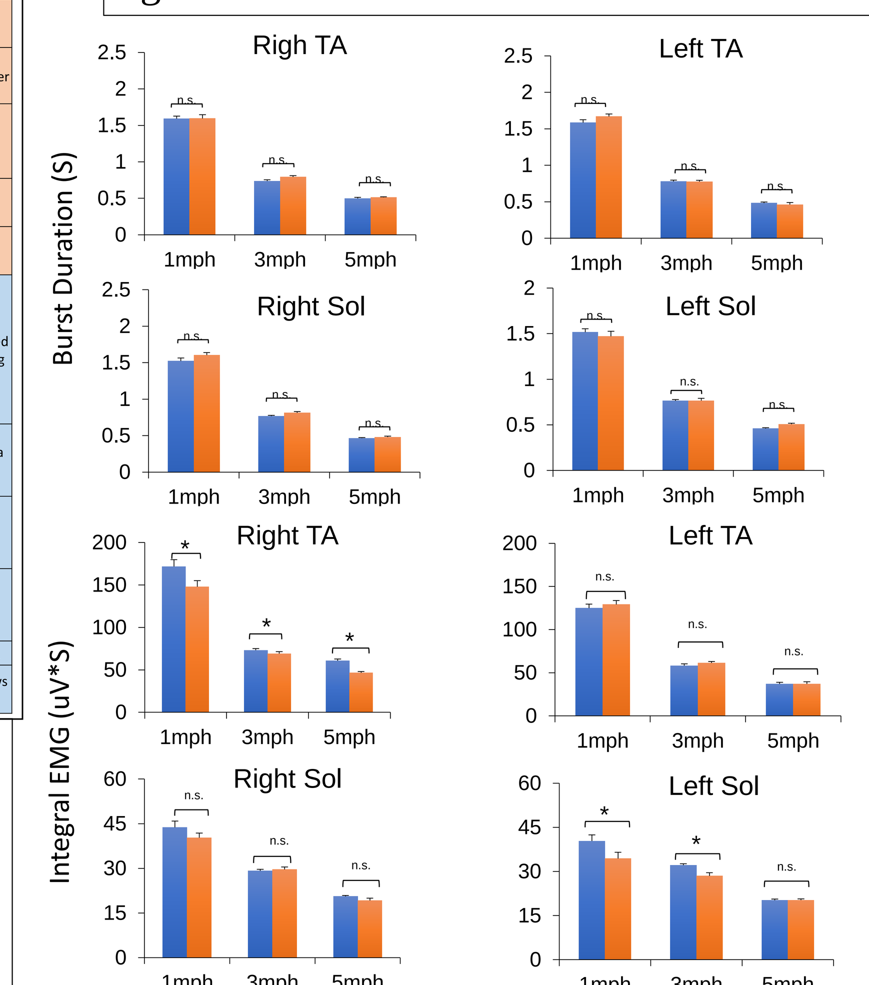

Fig 8. Burst duration and Integral EMG of tibialis anterior (TA) and soleus (Sol) muscles while stepping on treadmill without and with TSN. The spinal neuromodulation had no significant effect on burst duration and cycle period (data not show) at any speed in either the TA and Sol. There was a significantly (*) reduction in the EMG activity with TSN in the right TA at all speed and at 1 and 3 MPH in the left Sol.

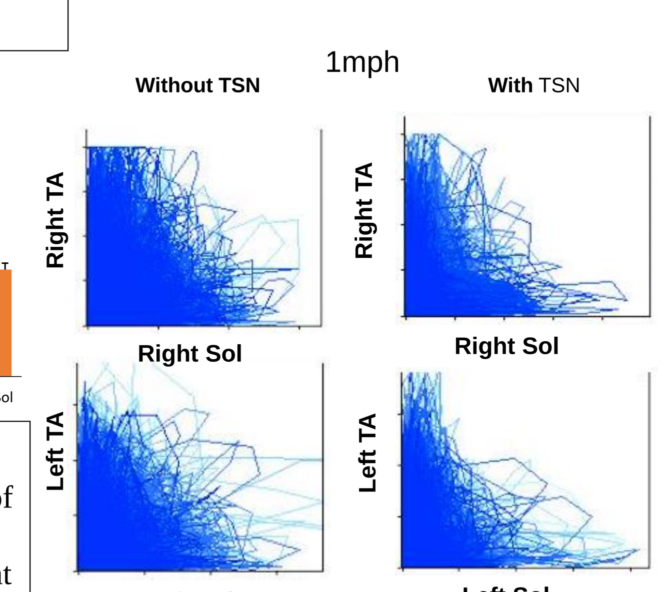

Fig 9. The amplitude of the EMG of the TA and soleus for each of the four plots generated during treadmill stepping at 1 mph without and with the TSN. For each graph a data point was derived consecutively every 10 ms for every step cycle. The data points are shifted significantly among the four quarters of the graph, consistent with a more normal agonists antagonists relationship between the TA and Sol in both the right and left leg as a result of a single period of neuromodulation.

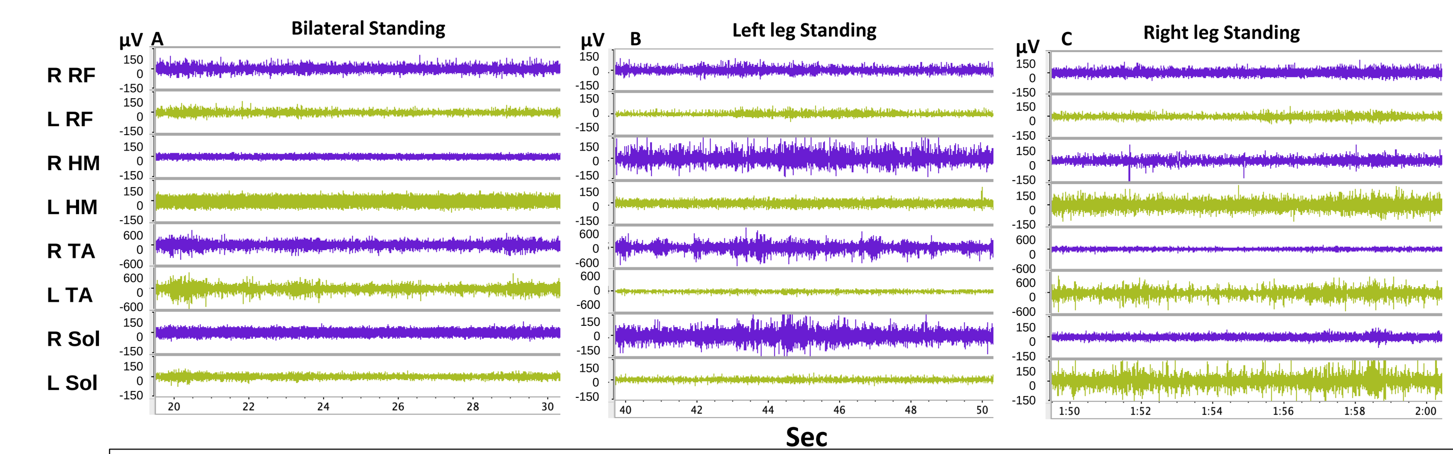

Fig 10. Representative sample of raw EMG signals during bilateral (A), left leg (B) and right leg (C) during a 10 sec period. RF, rectus femoris; HM, hamstring muscle.

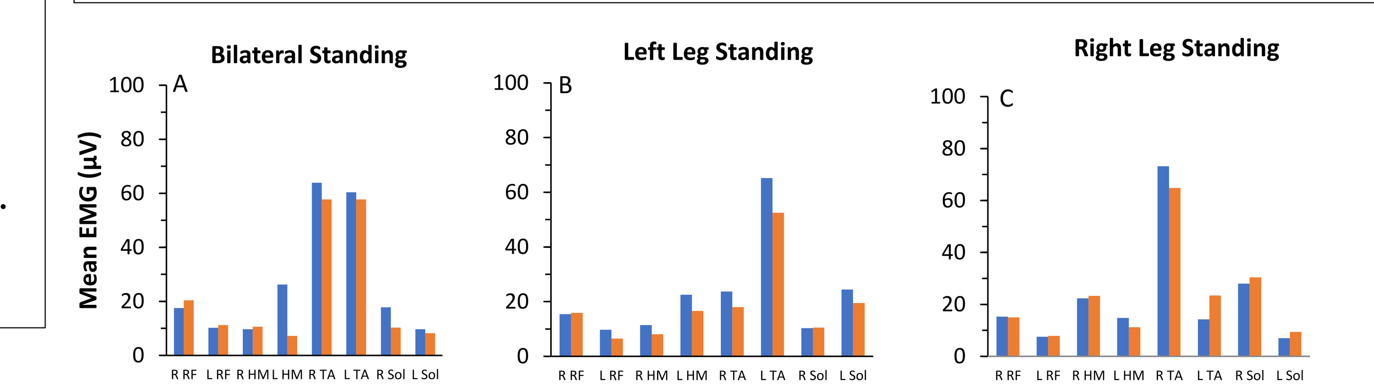

Fig 11. Mean EMG of the period while standing on both legs (A), on left leg only (B) and on right leg only (C). Note, mean EMG of TA muscles of the standing legs are more than two times higher than the other muscles. Note the reduction in mean EMG for the TA of the leg bearing the weight.

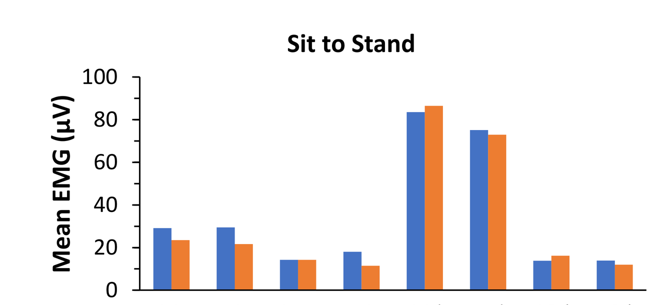

Fig 12. Mean EMG of the period of five sit-to-stands. Note, mean EMG of adductor muscles are more than two times higher than the other muscles.

SUMMARY

The plasticity necessary to achieve reorganization within and among different neural networks, was achieved with a combination of TSN and specific activity-dependent mechanisms. By engaging these two concepts we have demonstrated in a single patient a strategy that can lead to a successful adaptation of bidirectional reorganization of proprioception-spinal cord-brain connectivity to higher levels of functionality, without any invasive surgical or pharmacological interventions. **The major specific observations are**:

1. Multiple organ systems can be transformed noninvasively to higher functional states.

2. Fine sensory-motor skills as well as gross motor skills were improved.

3. Significant functional changes can occur within a single interventional treatment.

4. Small adjustments in the patterns of neuromodulation can have significant changes in functional outcomes.

ACKNOWLEDGMENTS

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