

Introduction

- **Dystonia** is a movement disorder with clinical features of involuntary intermittent or sustained muscle contractions [1].
- It is hypothesized that, a deficit of **inhibition** and abnormal plasticity within basal ganglia could be a key feature in the pathophysiology of dystonia [2].
- **Deep brain stimulation (DBS)** of basal ganglia has been proven useful for medically refractory dystonia [3].
- A previous study have demonstrated **depression** of local field evoked potentials in the basal ganglia output nuclei of dystonia patients using paired pulse stimulation [4].
- Paired-pulse stimulation paradigm has been greatly investigated using Transcranial Magnetic Stimulation but not much using DBS.

Methods

Patient: A 8 yo male diagnosed with Glutaric Aciduria type 1 (GA1), with hyperkinetic and hypertonic dystonia symptoms present in both sides.

Stereo electroencephalography (sEEG) leads: 5 externalized leads placed in following target regions in each hemispheres [4]:

- 2 leads in Globus Pallidus Internus (**GPI**)
- 1 lead through Ventral Oralis and Subthalamic Nucleus (**VoSTN**)
- 1 lead through Ventral Intermediate and Pedunculopontine nucleus (**VIMPPN**)
- 1 lead through Ventral Anterior nuclei (**VA**)

Paired-Pulse DBS: GPI_L stimulations were applied through low-impedance macro-contacts at 3 V, 90 us pulse width, 25 Hz with different inter-stimulus intervals (ISIs): 0.5, 1, 3, 5 ms

Patient: A 8 yo male diagnosed with Glutaric Aciduria type 1 (GA1), with hyperkinetic and hypertonic dystonia symptoms present in both sides.

Evoked potentials: Evoked potentials (EPs) were detected from recordings of VoSTN_L lead by averaging 1000 repetition of stimulation.

Fig. 1. The schematic of temporary leads implanted in target regions. Black squares represent macro stimulation contacts while little circles show 10 recording contacts.

9,10
7,8
4,5,6
1,2,3

Objectives

- In this preliminary study we want to investigate the inhibitory potentials of DBS paired-pulse stimulation on a dystonic patient.
- The result of this study can introduce kHz frequency stimulation settings as a potential future DBS system to induce inhibition for dystonic patients.

Conclusions

- Depending on inter-stimulus intervals, 2nd EP might:
 - ✓ Be **inhibited** completely (ISI 0.5 ms)
 - ✓ be a superposition of two EPs (ISI 1ms)
 - ✓ Have less amplitude than 1st EP (ISI 3ms)
 - ✓ Have higher amplitude than 1st EP (ISI 5ms)
- These results provides evidence for potential **clinical effects at stimulation frequencies above 1kHz.**
- More subjects are required to validate these results
- Future work will also investigate whether short ISI paired-pulse DBS could have inhibitory effects that differ from the effects of single-pulse continuous DBS.

Results (1)

Stimulation of GPI_L using different ISIs and recording from bipolar contact 4+5- of VoSTN_L

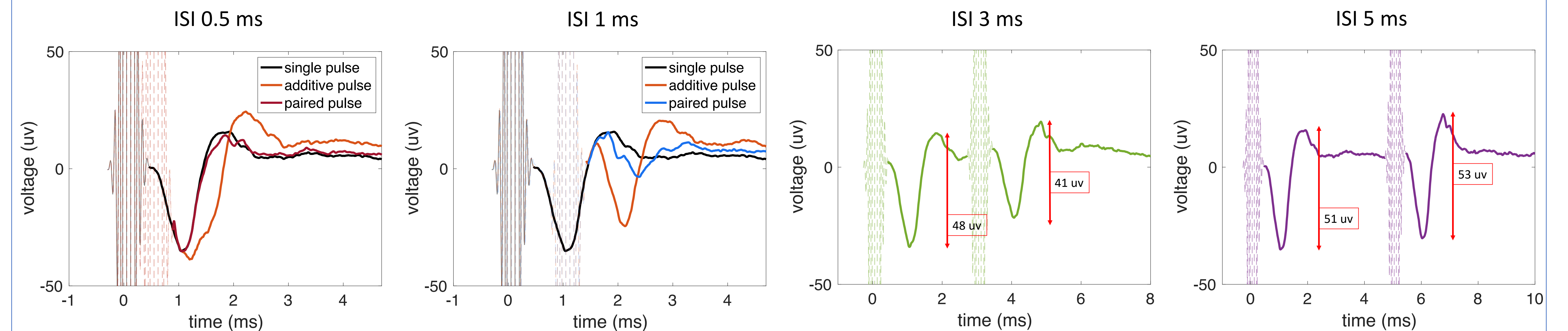


Fig. 2. EP generated by paired-pulse stimulation of ISI 0.5 ms is similar to EP of a single pulse stimulation if the stimulation would have been applied at time ~0. EP of paired-pulse is not like superposition of two ESs with time difference of 0.5 ms.

Fig. 3. EP generated by paired-pulse stimulation of ISI 1 ms is a bit different from EP of a single pulse stimulation if the stimulation would have been applied at time ~0. EP of paired-pulse is not like superposition of two EPs with time difference of 1 ms.

Fig. 4. Paired-pulse stimulation of ISI 3 ms has enough time to generate two independent EPs, however the second EP has less peak to peak amplitude comparing the first one.

Fig. 5. Paired-pulse stimulation of ISI 5 ms has enough time to generate two independent EPs, however the second EP has higher peak to peak amplitude comparing the first one.

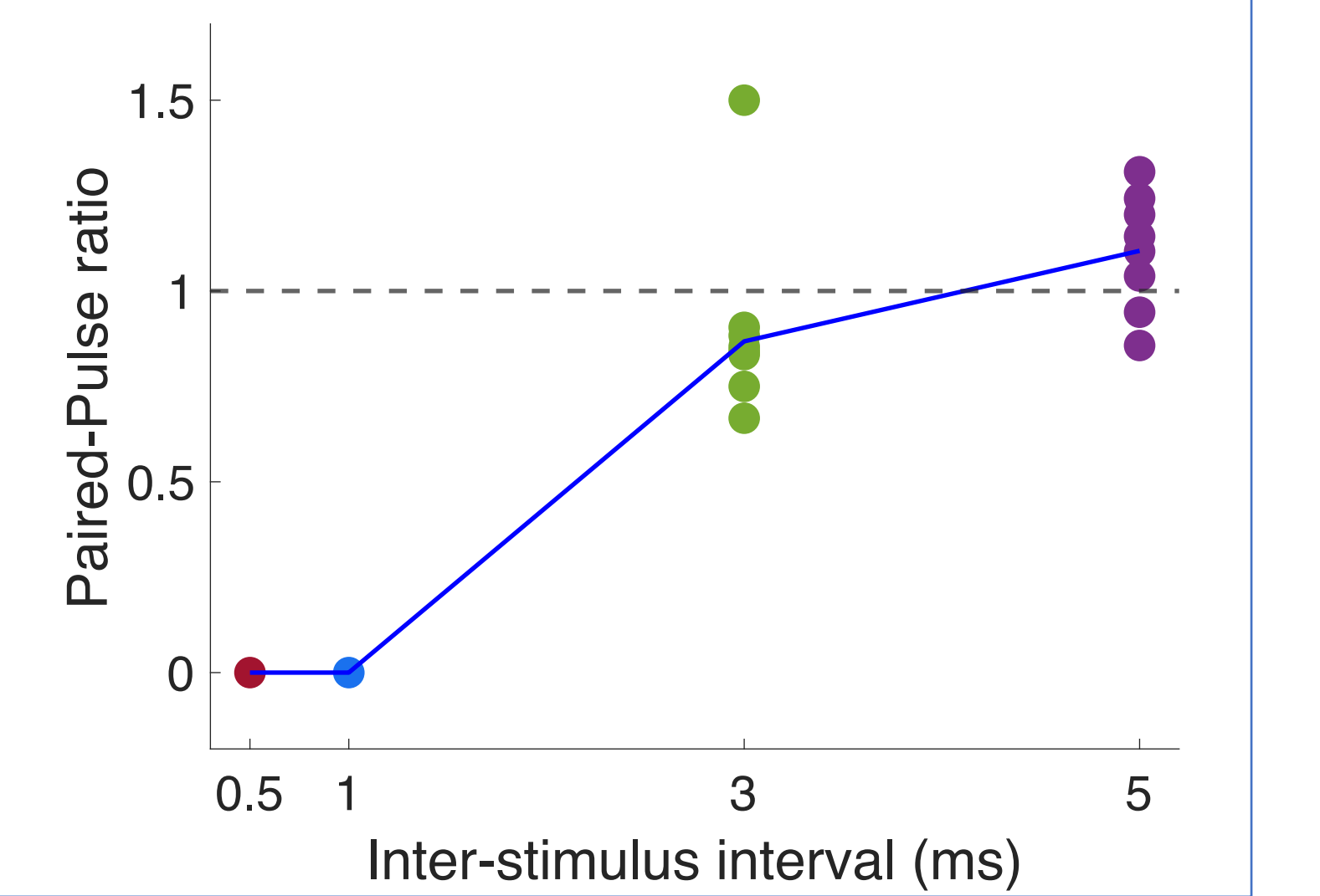
Results (2)

Paired-Pulse Ratio (PPR)

$$PPR = \frac{\text{Peak to Peak amplitude of 2nd EP (uv)}}{\text{Peak to Peak amplitude of 1st EP (uv)}}$$

- No 2nd EP in ISI 0.5 and 1 ms -> PPR = 0
- Average PPR of all contacts in ISI 3ms is less than 1
- Average PPR of all contacts in ISI 5ms is higher than 1

Fig. 6. The PPR of bipolar recordings of Vo_STN_L when GPI1_L is stimulated. 8 circles at each ISI correspond to 8 bipolar recording contacts. All circles at ISI 0.5 and 1 are on top of each other.



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