

# Deep Brain Stimulation Targets for the Treatment of Dystonic Tremor

Lan Luo, MD and Joohi Jimenez-Shahed, MD

Parkinson's Disease Center and Movement Disorders Clinic, Department of Neurology  
Baylor College of Medicine, Houston, Texas

## BACKGROUND

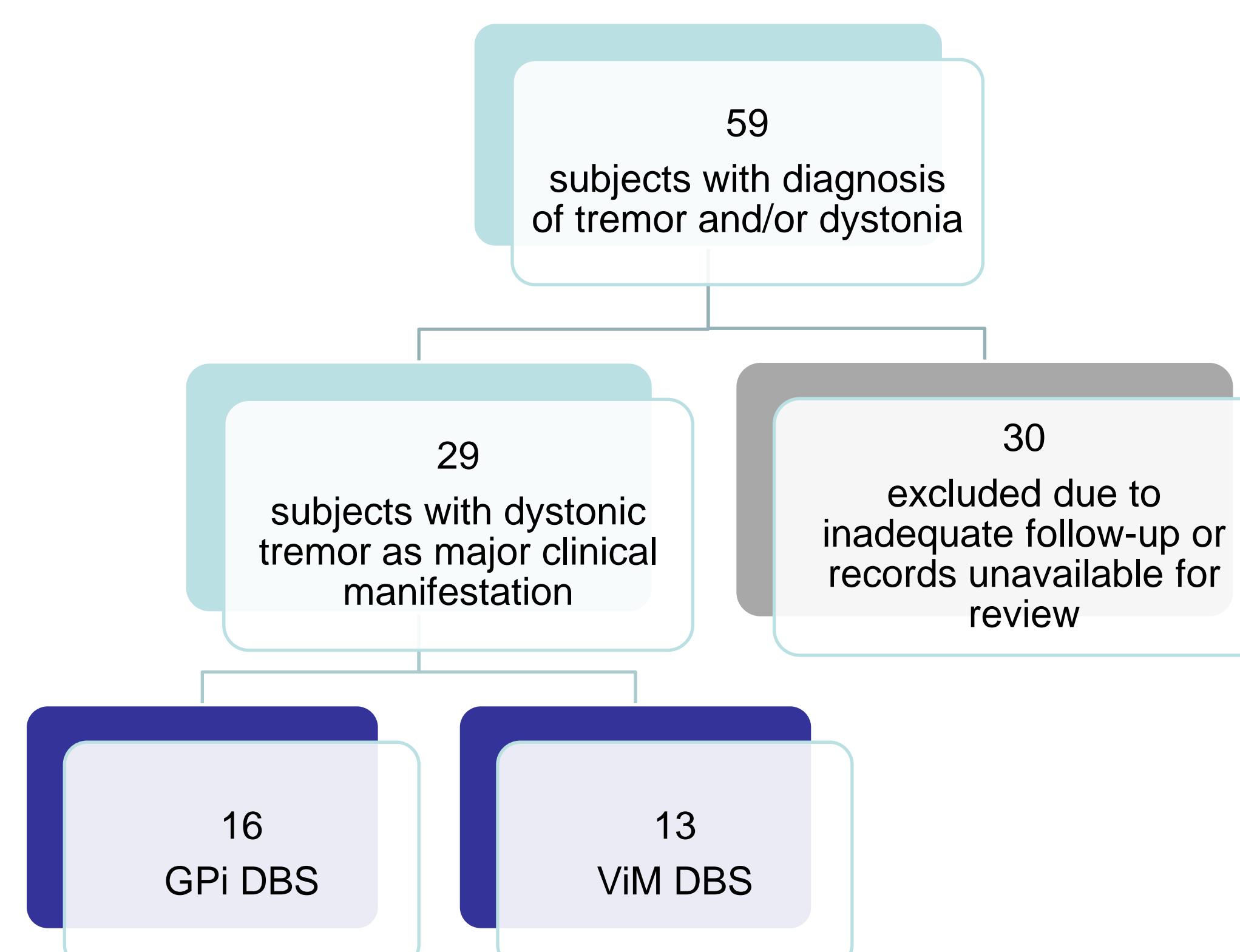
- ❖ Dystonia is characterized by sustained, repetitive, patterned contractions of opposing muscles groups which result in abnormal postures or twisting movements<sup>1</sup>.
- ❖ Dystonia can be classified anatomically into either focal, segmental, multifocal, hemidystonia, or generalized dystonia. Features of dystonia can also include dystonic tremor (DT).
- ❖ DT has the following key characteristics<sup>2</sup>:
  - associated with a dystonic posture
  - irregular amplitudes and frequency (usually <7Hz)
  - postural-intentional tremor rather than resting tremor.
- ❖ Tremor associated with dystonia (DAT) is often used to describe dystonic tremor when present in a body region not affected by dystonia, with dystonia present elsewhere in the body<sup>3</sup>.
- ❖ Dystonia associated dystonic tremor (DADT) is a term used to describe dystonic tremor which is present in the same anatomical location as the dystonia.
- ❖ A few small case series have described the posterior subthalamic area<sup>4</sup>, the caudal zona incerta nucleus<sup>5</sup>, globus pallidus interna<sup>6,7,8</sup>, and the ventral intermediate nucleus of the thalamus<sup>7,8,9,10</sup> as potential surgical targets for the treatment of dystonic tremor. There is limited information in the scientific literature regarding DBS for the treatment of medication refractory dystonic tremor.

**❖ OBJECTIVE:** To describe the efficacy of thalamic (ViM) and pallidal (GPI) deep brain stimulation for the treatment of medication-refractory primary DT.

## METHODS

- ❖ We retrospectively identified patients with a diagnosis of dystonia and/or tremor from our DBS database (subjects implanted between 1/1996-3/2013).
- ❖ Inclusion criteria:
  - clinical diagnosis of dystonia in whom a major disease manifestation is tremor
  - patients treated with ventral intermediate nucleus (ViM) thalamic or pallidal (GPI) deep brain stimulation for the treatment of dystonic symptoms.
- ❖ Exclusion criteria:
  - subjects with secondary dystonic tremor
- ❖ Demographic variables, age at onset of symptoms, anatomical distribution of tremor and dystonia, symptom duration at time of surgery, DBS-related variables, total duration of follow-up, medications used for tremor pre- and post-op were all recorded.
- ❖ Change in dystonia and tremor symptoms at the last clinic visit compared to baseline was rated on a scale of 0-2 (0= no improvement, 1= some improvement, 2= marked improvement) based on chart review.

**Figure 1: Patients included in analysis**



## RESULTS

**Table 1: Patient characteristics and DBS variables**

	GPI group (n= 16)	ViM group (n= 13*)
Avg. current age (in yrs)	57.3 ±16.1	68.8±9.4
Sex	9M, 7F	7M, 6F
Avg. age at symptom onset (yrs)	33.0 ±21.3	36.7 ±20.9
Avg. age at DBS implantation (yrs)	50.2 ±18.1	62.2 ±7.6
Avg. pre-operative symptom duration (yrs)	17.2 ±10.3	25.5 ±16.0
Avg. post-surgical follow-up (yrs)	3.1 ±2.8	3.6 ±3.7
Unilateral electrode placement	0	7**
Bilateral electrode placement	16	6

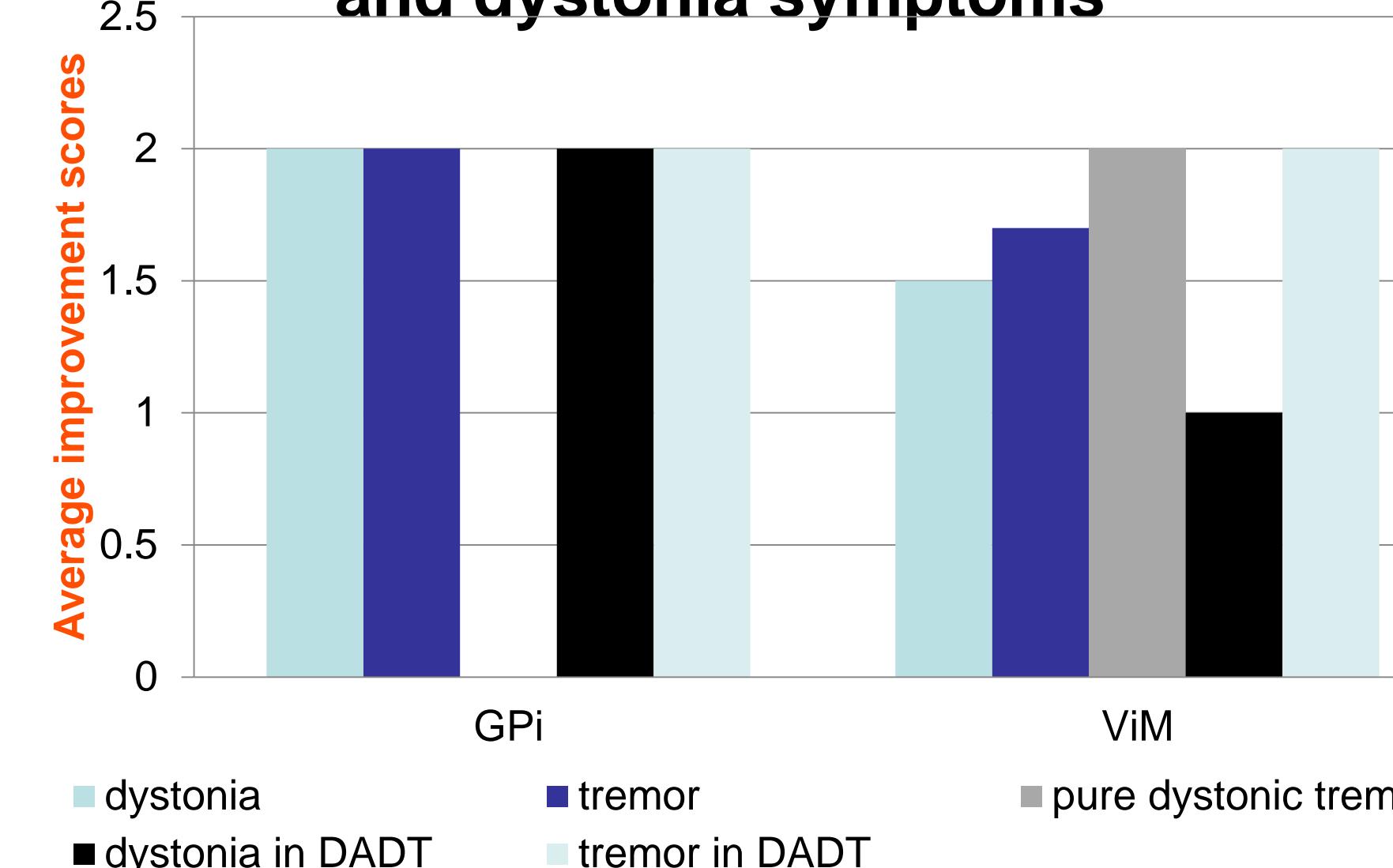
\*One patient had ineffective bilateral GPI DBS followed by bilateral ViM DBS placement (GPI electrodes inactivated).

\*\*One patient had bilateral ViM DBS placement but has only right ViM active due to adverse stimulation events associated with left ViM.

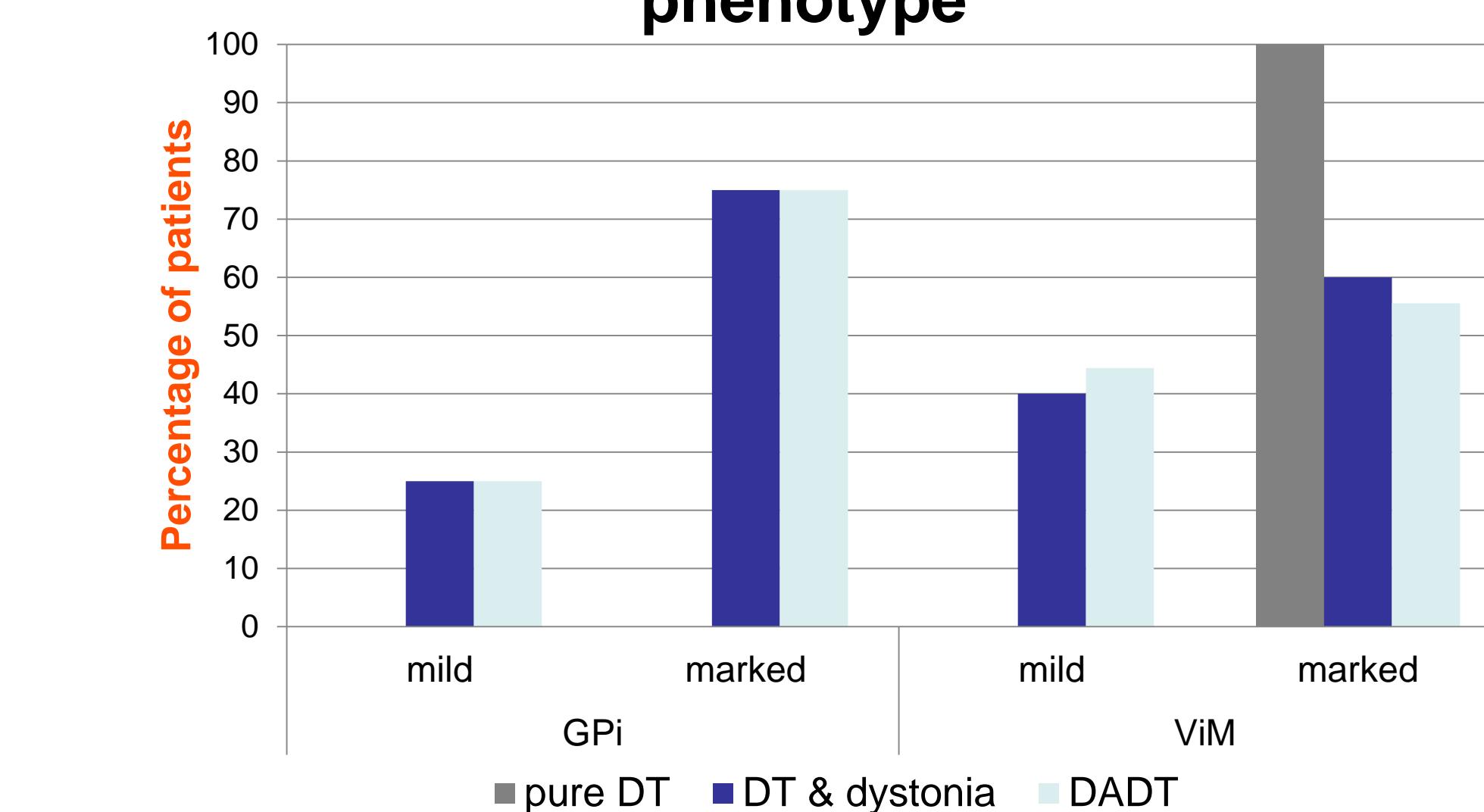
**Table 2: Anatomical distribution of dystonia and dystonic tremor**

	GPI			ViM		
	Dystonia	Tremor	Dystonic tremor	Dystonia	Tremor	Dystonic tremor
Focal	6	15		3	11	
Head	6	9		2	3	
Arm/hand	0	6		1	8	
Segmental	2	1		4	2	
Multifocal	2	0		1	0	
Hemi-body	0	0		1	0	
Generalized	6	0		1	0	
No dystonia	0	--		3	--	
			N=16			
			DADT			
					TAD	
					N=1	
					DADT	
					N=9	
					Pure DT	
					N=3	

**Figure 2: Average improvement in tremor and dystonia symptoms**



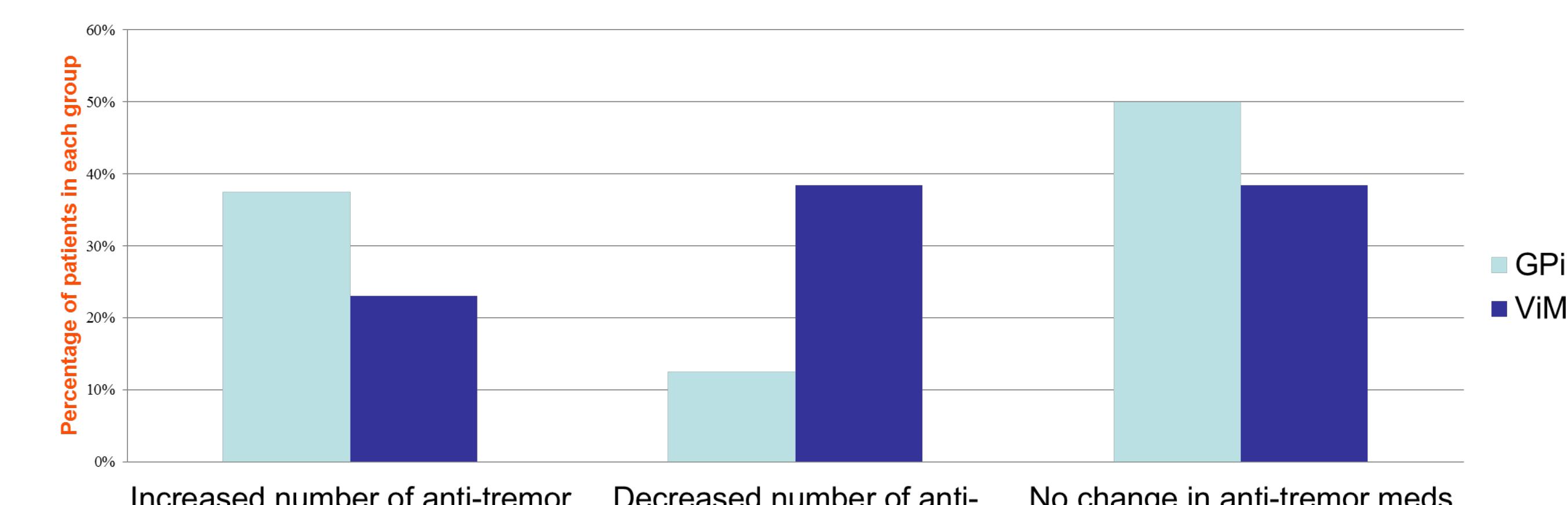
**Figure 3: Improvement in dystonic tremor by phenotype**



**Table 3: DBS parameters (per electrode)**

	GPI	ViM
Avg. amplitude (V)	3.7 ±1.2	3.4 ±0.8
Avg. pulse width (usec)	138.8 ±47.3	154.7 ±26.8
Avg. frequency (Hz)	160.0 ±110.4	96.8 ±59.3

**Table 4: Change in tremor medications after DBS**



## DISCUSSION

- ❖ We found greater improvement in dystonia in the GPI group when compared to the ViM DBS group. Additionally, there was greater improvement in DT in those who underwent GPI DBS.
- ❖ Subgroups of DT may respond differently to DBS
  - Subjects with DADT were more likely to have undergone GPI DBS
  - Subjects with pure DT were all treated with ViM DBS
- ❖ There was greater improvement in subjects with DADT (whose dystonia and dystonic tremor presented at the same anatomical location) who were stimulated using Gpi DBS
  - Since dystonic tremor is often observed along with dystonia, perhaps the improvement in this DT subtype can be linked to a corresponding improvement in dystonia in the pallidal DBS group.
- ❖ Three patients with pure DT were stimulated with ViM DBS group and all had marked improvement in tremor.
  - Previous authors<sup>9</sup> have also suggested ViM DBS is the better target for patients with DT whose main phenotype is tremor. However, their cohort of patients did not include any patients with pure DT.
- ❖ There was only one patient with TAD in our cohort
- ❖ Our findings favor pallidal DBS for DT, which supports prior studies suggesting that the optimal surgical target for dystonia is the globus pallidus<sup>10, 11</sup>. However, our finding in favor of pallidal DBS for DADT deviates from prior smaller studies suggesting thalamic DBS may be a better target.
  - However, a higher percentage of patients in the pallidal DBS group increased the number of anti-tremor medications post-operatively.
- ❖ Strengths of the study included:
  - Large patient cohort with primary dystonic tremor.
  - Similar baseline characteristics between both groups.
- ❖ Limitations to the study included:
  - Choice of DBS targets for implantation was not randomized and therefore could lead to selection bias.
  - A portion of cohort had limited follow-up information or records were unavailable for review.

**❖ CONCLUSION:** Prospective analysis evaluating the efficacy of thalamic and pallidal DBS for the treatment of medication-refractory primary dystonic tremor is currently ongoing.

## REFERENCES

- Albanese A, Jankovic J. Hyperkinetic Movement Disorders: Differential Diagnosis and Treatment. Chichester: Wiley-Blackwell; 2012.
- Deuschl G, Bain P, Brin M; Consensus statement of the movement disorder society on tremor: ad hoc scientific committee. *Mov Disord* 1998; 13(suppl 3):2-23.
- Fasano A, Bove F, Lang AE. The treatment of dystonic tremor, a systematic review. *J Neurol Neurosurg Psychiatry*. 2013;0:1-11.
- Jung BA, Park MK, Lee WH, Ghang CG. Deep brain stimulation of the subthalamic area for dystonic tremor. *Journal of Korean Neurosurgical Society* 2009;45:303-305.
- Plaha P, Khan S, Gill SS. Bilateral stimulation of the caudal zona incerta nucleus for tremor control. *J Neurol Neurosurg Psychiatry* 2008;79:504-513.
- Iessar MM, Hedera P, Phibbs FT, Konrad PE, Neimat JS. Treating post-traumatic tremor with deep brain stimulation: report of five cases. *Parkinsonism Relat Disord* 2013;19:1100-5.
- Moishisita T, Foote KD, Haq IU, Zeilman P, Jacobson C, Okun MS. Should we consider Vim Thalamic Deep Brain Stimulation for Select Cases of Severe Refractory Dystonic Tremor. *Stereotact Funct Neurosurg* 2010;88:98-104.
- Hedera P, Phibbs FT, Dolhin R, Charles PD, Konrad PE, Neimat JS, Davis TL. Surgical targets for dystonic tremor: Considerations between the globus pallidus and ventral intermediate thalamic nucleus. *Parkinsonism Relat Disord* 2013;19:684-686.
- Racette BA, Dowling J, Randle J, Mink JW. Thalamic stimulation for primary writing tremor. *J Neurol* 2001;248:380-2.
- Kuncel AM, Turner DA, Ozelius LJ, Greene PE, Grill WM, Stacy MA. Myoclonus and tremor response to thalamic deep brain stimulation parameters in a patient with inherited myoclonus-dystonia syndrome. *Clin Neurol Neurosurg* 2009;111:303-6.
- Krauss JK. Deep brain stimulation for dystonia in adults. *Stereotact Funct Neurosurg* 2007;78:168-182.
- Ostrem JL, Starr P. Treatment of dystonia with deep brain stimulation. *Neurotherapeutics*. 2008; 5:320-330.