

# DEEP BRAIN STIMULATION FOR TOURETTE SYNDROME

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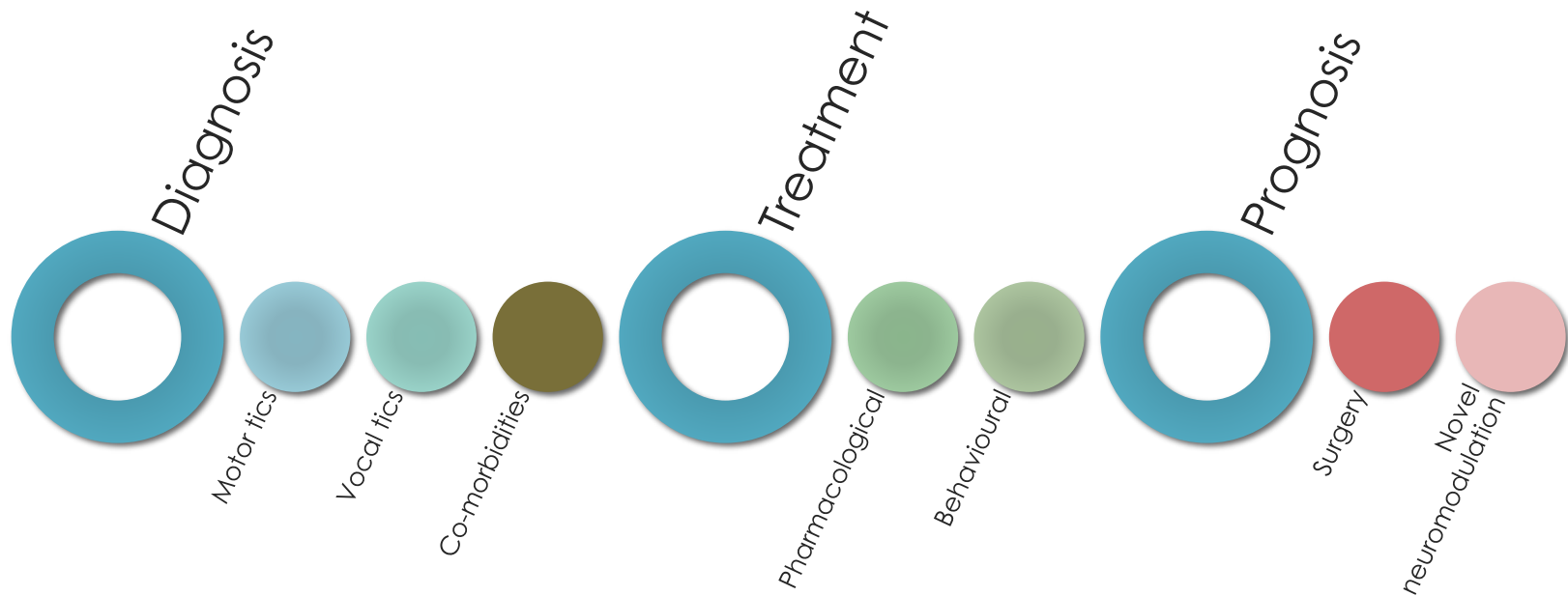
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# The success story of DBS in Movement Disorders

- Proven therapeutic effect in disabling conditions
  - Need for another therapy
  - Safe side-effect profile
  - Improvement of QoL
- Patient selection
  - The (almost) ideal patient
- Management of programming and medication adjustment
  - Long term commitment (clinician)



# Gilles de la Tourette Syndrome



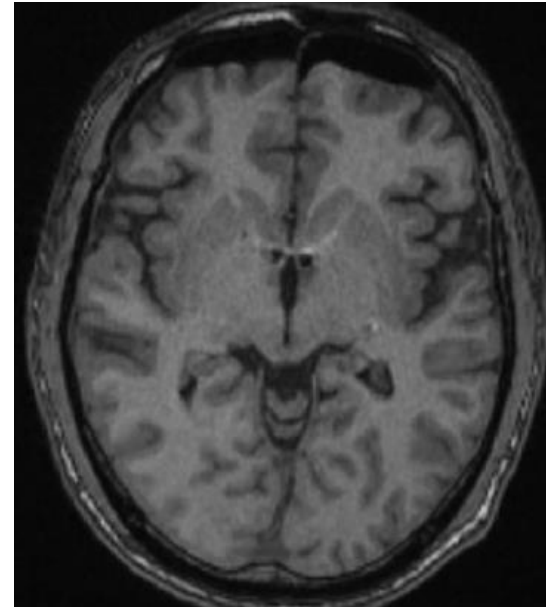
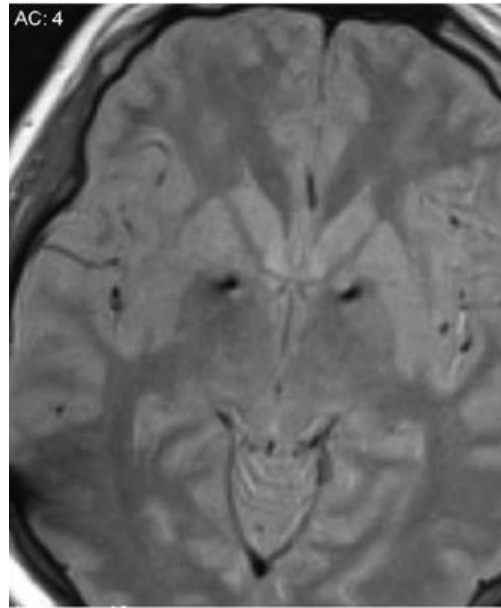
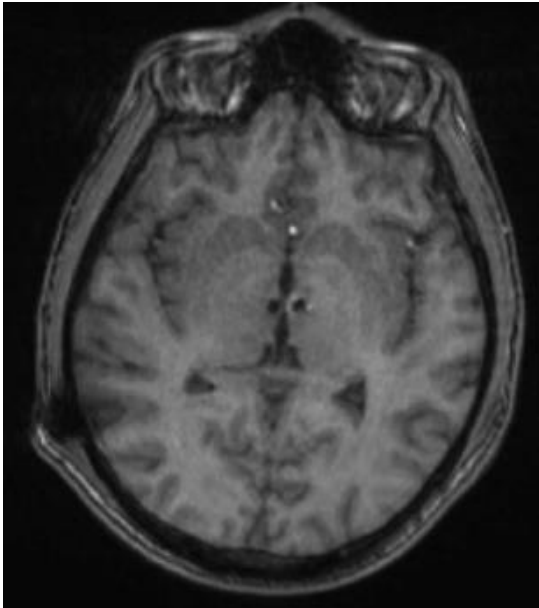
# DBS in Tourette syndrome

## Conflict in the numbers

- Outcome data
  - Level of evidence – RCT vs. Open label
- Target selection debate
  - Thalamus vs. Pallidum
    - Anteromedial pallidum vs. posteroventral pallidum
    - Centro-median vs. anterior Th
- Co-morbidity identification and treatment
- Selection process / criteria necessary



# Is there a best target?



# Is there a best target?

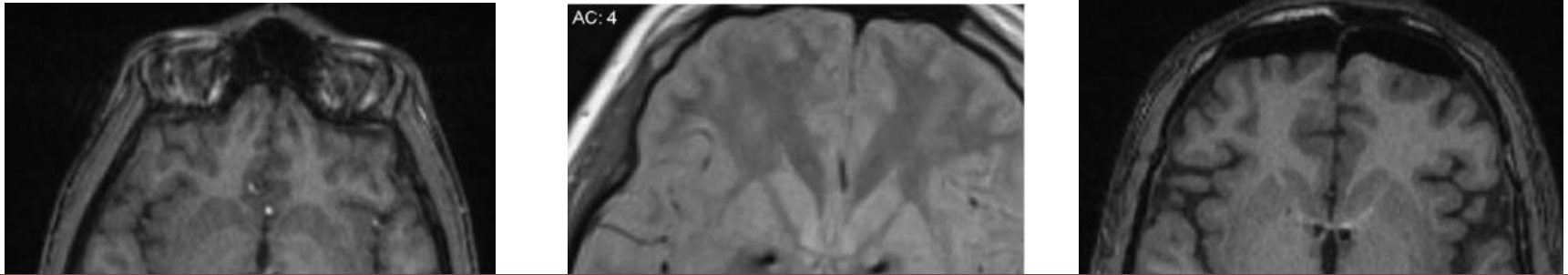
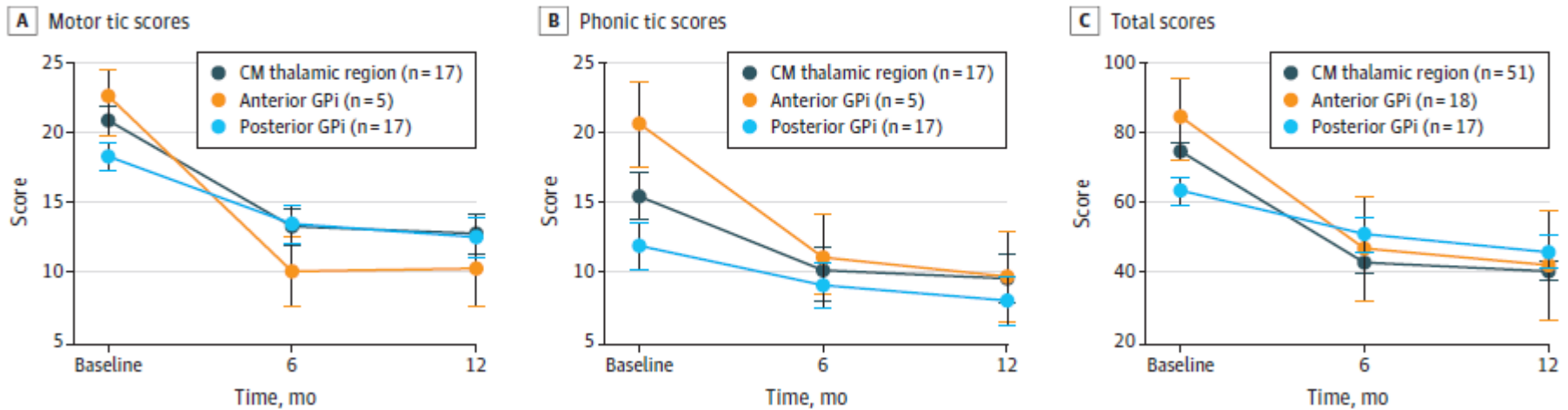
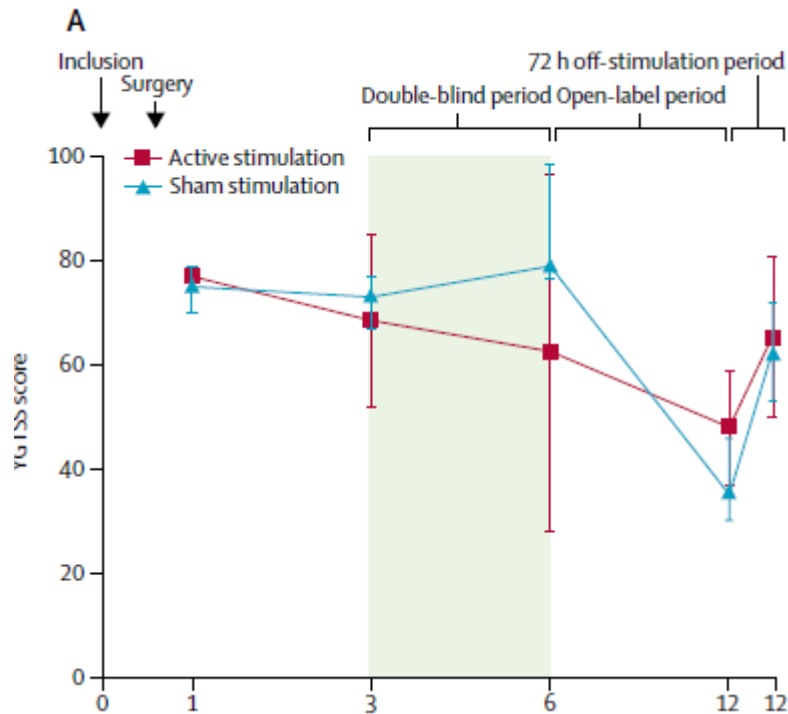


Figure. Yale Global Tic Severity Scale (YGTSS) Scores by Time and Brain Target

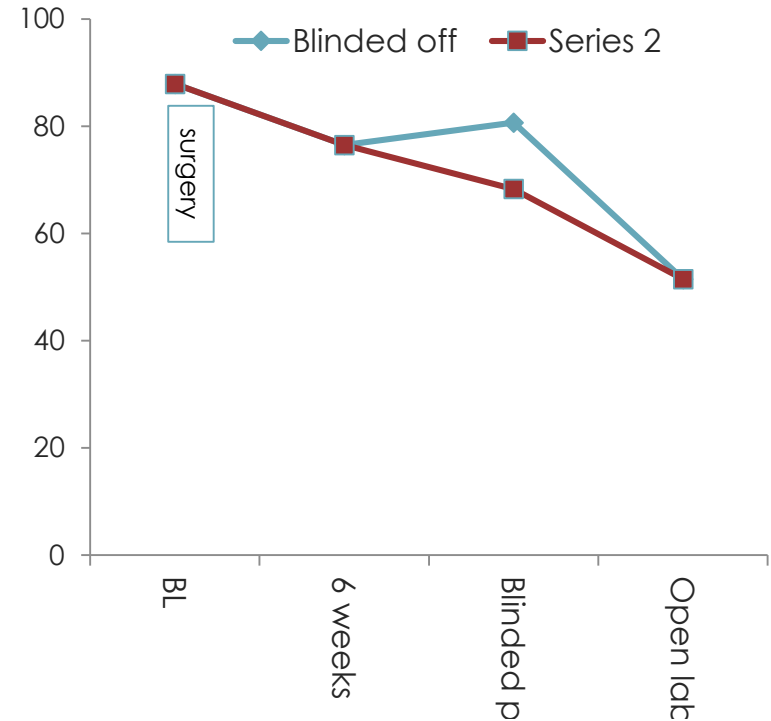


# Outcomes – amGPi - RCT



## Anterior pallidal deep brain stimulation for Tourette's syndrome: a randomised, double-blind, controlled trial

Marie-Laure Welter, Jean-Luc Houeto, Stéphane Thobois, Benoit Bataille, Marc Guenet, Yulia Worbe, Andreas Hartmann, Virginie Czernecki, Eric Bardinet, Jerome Yelnik, Sophie Tezenas du Montcel, Yves Agid, Marie Vidailhet, Philippe Cornu, Audrey Tanguy, Solène Ansqer, Nematollah Jaafari, Emmanuel Poulet, Giulia Serra, Pierre Burbaud, Emmanuel Cuny, Bruno Aouizerate, Pierre Pollak, Stephan Chabardes, Mircea Polosan, Michel Borg, Denys Fontaine, Bruno Giordana, Sylvie Raoul, Tiphaine Rouaud, Anne Sauvaget, Isabelle Jalenques, Carine Karachi, Luc Mallet, for the STIC study group\*



## Bilateral globus pallidus stimulation for severe Tourette's syndrome: a double-blind, randomised crossover trial

Zinovia Kefalopoulou, Ludvic Zrinzo, Marjan Jahanshahi, Joseph Candelario, Catherine Milabo, Mazda Beigi, Harith Akram, Jonathan Hyam, Jennifer Clayton, Lewis Kass-Iliyya, Monty Silverdale, Julian Evans, Patricia Limousin, Marwan Hariz, Eileen Joyce, Thomas Foltynie



**TABLE 2. Patient Selection for DBS in GTS: Synthesis of Outlined Criteria Used in Clinical Studies and Recommendations From the Literature<sup>a</sup>**

	Inclusion Criteria	Exclusion Criteria
Mink et al (2006) <sup>67</sup>	<p><b>DSM-V diagnosis of TS by expert clinician</b></p> <ol style="list-style-type: none"> <li>1. Age is not a strict criterion</li> <li>2. Local ethics committee involvement for cases &lt; 18 years old</li> <li>1. Severe tic disorder with functional impairment</li> <li>2. YGTSS &gt; 35/50</li> <li>3. Document with standardized video assessment</li> <li>1. Tics should be the major symptom causing disability</li> <li>2. Comorbid conditions should be stably treated</li> <li>3. Comorbid conditions should be assessed using valid rating scales when available</li> <li>1. Failed treatment trials from 3 pharmacological classes: a) alpha-adrenergic agonist, b) 2 dopamine antagonists (typical &amp; atypical), c) a drug from at least one additional class (eg, clonazepam, amphetamine, or clonidine)</li> <li>2. A trial of CBIT should be offered</li> </ol> <p><b>Stable for 6 months before DBS</b></p> <ol style="list-style-type: none"> <li>1. Adequate social support without acute or sub-acute psychosocial stressors</li> <li>2. Active involvement with psychological interventions when necessary</li> <li>3. Caregiver available to accompany patient for frequent follow-up</li> <li>4. Psychogenic tics, embellishment, factitious symptoms, personality disorders, and malingering must be recognized and addressed</li> </ol> <p><b>Documentation of no active SI/HI for 6 months</b></p> <ul style="list-style-type: none"> <li>• Compliance to previous interventions</li> <li>• Able to provide consent</li> <li>• Able to withstand surgery</li> </ul>	<p>disorder due to other medical, neurological, or psychiatric disorders</p> <p>Severe medical, neurological, psychiatric, cognitive disorders</p> <p>Not likely to benefit from neurosurgical interventions</p> <p>Significant psychosocial factors that increase risk of surgical procedure or prevent recovery and outcome</p> <p>Assessment (eg, noncompliance to previous interventions, history of multiple surgical procedures)</p> <p>Unwilling to be involved in ongoing psychological interventions or treatments</p> <p>High risk factors</p> <p>Significant brain lesions determined by neuroimaging</p> <p>Significant dementia</p> <p>History of head trauma before tic onset</p> <p>History of dopamine blockers before tic onset</p> <p>Previously implanted electrical device within previous 24 mo</p> <p>Failed surgical attempt within previous 12 mo</p> <p>Significant sociopathic personality disorder or planned pregnancy</p> <p>Disorder other than GTS</p> <p>Severe psychiatric comorbidities other than associated behavioural disorders</p> <p>Intellectual deficiency</p> <p>Severe cardiovascular, pulmonary or hematological disorders</p> <p>Structural abnormalities as revealed by neuroimaging</p> <p>Active suicidal ideation</p> <p>Diagnosis of DSM Axis I disorder</p> <p>Alcoholism</p> <p>Alcohol-related or iatrogenic tic disorder</p> <p>Failed attempts at medical treatment</p> <p>Cognitive dysfunction</p> <p>Severe depression</p> <p>Non-compliance</p> <ul style="list-style-type: none"> <li>• Substance abuse</li> <li>• Unable to withstand surgery (previous brain surgery, poor medical condition)</li> <li>• Abnormal neuroimaging results</li> </ul>
Maciunas et al (2007) <sup>72</sup>		
Ackermans et al (2008) <sup>69</sup>		
Porta et al (2009) <sup>68</sup>		

Confirmed diagnosis

Age

Severity

- Grading / Score
- Impairment
- Life threatening

Failed treatment

- Drugs
- Psychotherapy

Psychiatric comorbidity

Social support



# DBS IN TOURETTE SYNDROME OUR EXPERIENCE WITH 6 CASES

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Pretoria DBS centre

# Demographic profile

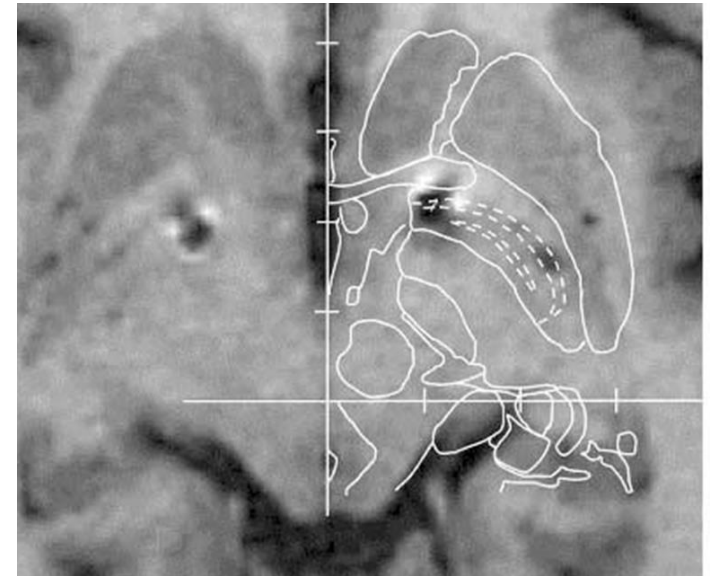
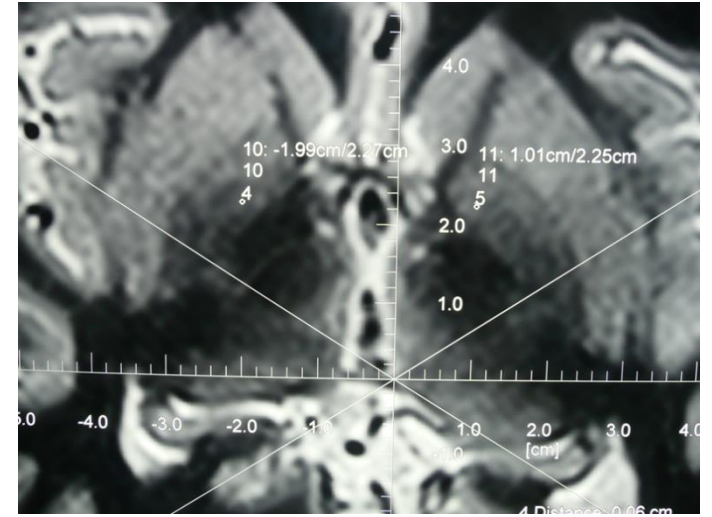
Patient	Gender	AAO	AGE AT Surgery	Family history TS
AD	Male	12	33	None
DG	Male	12	16	None
KH	Female	7	16	Positive
SB	Male	6	26	Positive
BR	Male	11	24	Positive
WO	Male	12	25	Positive

# Pre-surgical characteristics

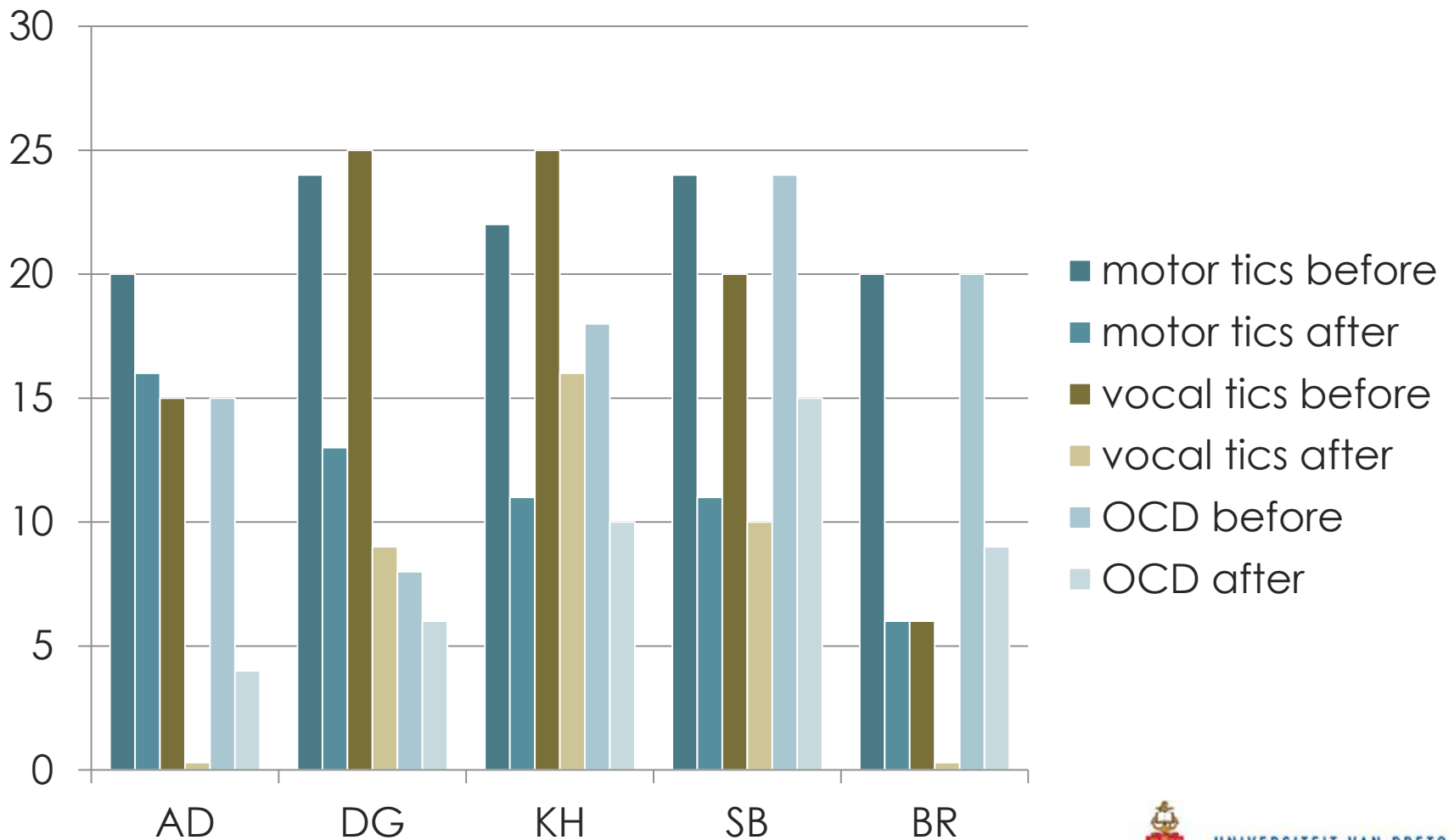
	Motor tics	Vocal tics	Self injury	OCD	Other	# of drugs	Target
AD	++	++	-	++	None	2	Am-GPi
DS	+++	+++	+++	++	ADD / AI	5	Am-GPi
KH	+	+++++	-	+	ADD	4	Am-GPi
SB	+++	++	+++	+++	Anxiety	5	Am-GPi
BR	++	+	++	++	ADD	4	Am-GPi
WO	++	+	+++	++	Autism	4	VS/ALIC



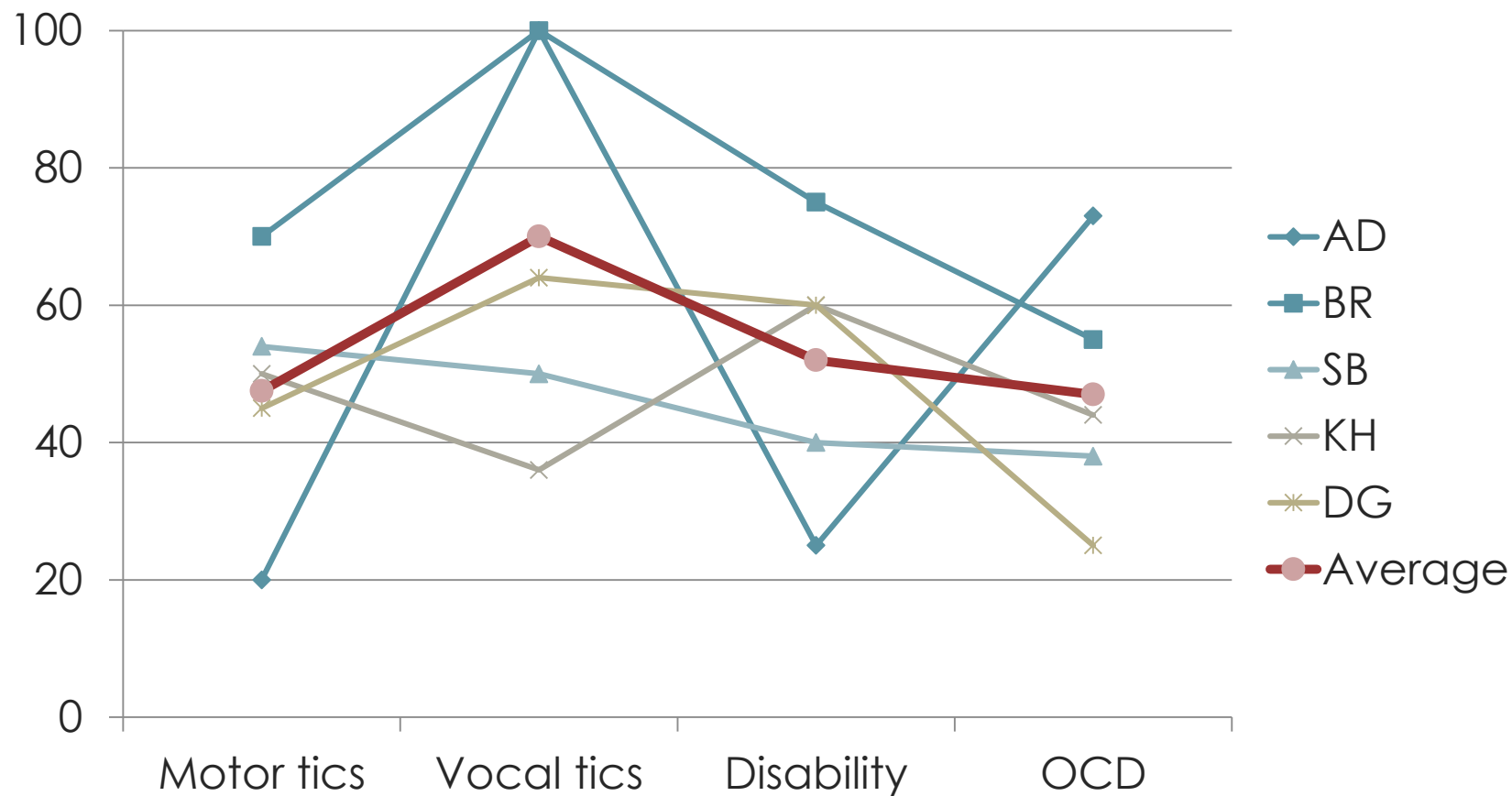
# Antero-medial GPi



# DBS Outcome – individual patients



# Percentage improvement after DBS



# Disability

Patient	Comment	Disability score – Yale TSI	Self injury	Comment	Score	Self injury
AD	Unable to work	40		Return working	30	
DG	Unable school	50	+++	Back to school	20	+
KH	Unable to school	50		Improvement	20	
SB	Left school – grd 8	50	+++	Improved fx	30	o
BR	Poor work performance	40		Much improved	20	
WO	Low level of function	40	+++	Improv insight	30	o (+)



# DBS

## Stimulation settings

Pt	1 <sup>st</sup> FU	1 <sup>st</sup> FU mA	Last FU	Last FU mA
AD	0- C+	4.0	0- 2+	2.0
DG	0- C+	3.0	0- 1- C+	3.5
KH	0- C+	3.5	0- 1- C+	4.0
SB	1- C+	3.5	0- 1- C+	5
BR	1- C+	4.0	0- 1- C+	3.2

PW 60 – 90us (AD at FU 120us)  
F 130Hz

## Adverse events

- Surgical
  - One patient had repositioning to assist charging of RC
  - We had no device related infections
- Stimulation induced
  - Agitation / dysphoria
  - Hypomania
    - Suicidal ideation (2- c+; 10- c+)





# Challenges with Follow-up

- Management of medication
  - Which drugs to stop when?
- Behavioural and psychiatric problems
  - Role of psychiatrist in follow up and selection
- DBS settings
  - Contact choice – ventral vs. dorsal
  - Best settings – mA, us, Hz
  - Regular adjustments – frequent follow up visits
- Adjustment to normality
  - Family and patient
  - Expectations

# Acknowledgements

- Patients and their families
- Pretoria DBS team
  - Pieter Slabbert (neurosurgeon)
  - Elsa Lubbe (paediatric neurologist)
  - Nafisa Cassimjee (neuropsychologist)
  - Raven Kisten (registrar – neurology)
    - Nico Enslin (neurosurgeon Red Cross Children's hospital)
- Medtronic South Africa
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  - Janardan Vaidyanathan
  - Brendan Pepper

