Patient selection for surgery: Hyperkinetic movement disorders

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Hyperkinetic Movement Disorders

- Tremor
- Dystonia
- Myoclonus
- Chorea
- Tics
Tremor

- Involuntary rhythmic oscillation of one or several body parts
- Heterogeneous etiology, symptom and disease entity
- First approved indication for DBS with 3 decades of clinical experience
## Activation conditions and frequencies

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Frequency range</th>
<th>Activation by</th>
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<td></td>
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<td>rest</td>
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<tr>
<td>Enhanced physiologic tremor</td>
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<td>Essential tremor syndromes</td>
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<td>Classical essential tremor</td>
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<td>Primary orthostatic tremor</td>
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<td>Task and position specific tremor</td>
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<td>Unclassified tremor</td>
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<td>Dystonic tremor</td>
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<td>Parkinsonian tremor</td>
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<td>Cerebellar tremor</td>
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<td>Holmes tremor</td>
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<td>Palatal tremor</td>
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<td>Neuropathic tremor</td>
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<td>Toxic and drug-induced tremor</td>
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<td>Psychogenic tremor</td>
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- **Typical frequencies**
- **Rare frequencies**
- **Necessary for diagnosis**
- **May occur**

Elble and Deuschl, MDJ 2011
Tremor analysis

- Functional tests (spiral drawing)
- Tremor scales
  - Fahn–Tolosa–Marin (FTM) Skala
  - Webster Scale (VI: 0-4)
  - TETRAS (The Essential Tremor Rating Scale)
  - TRS (tremor rating scale)
- UPDRS III (tremor subscale)
- Accelerometry
- EMG
- MEG-EMG coherence analysis
Tomography of power and coherence with MEG and beamformer analysis

„Dynamic Imaging of Coherent Sources“

Gross and Schnitzler, Nat Rev Neurosci 2005
Common patient selection criteria for DBS

• Reach correct diagnosis
  – Is it tremor? (or ataxia, myoclonus)
  – What kind of tremor? (exclude functional tremor)

• Tremor condition is functionally disabling and/or severely stigmatizing

• Medical treatment proved insufficient

• No contraindication for DBS surgery (significant comorbidities, brain atrophy, age)
Essential tremor

- Most frequent movement disorder (1-6%)
- Posture, action, intention
- Hands (95%), head 35%, voice 15%, legs 10%, trunk 3%
- Frequency 4-12 Hz
- 50% responsive to alcohol intake
- 50-60% positive family history
ET: Diagnostic workup

- Neurological examination
- Lab exams
- Tremor analysis
- MRI Scan
- DAT Scan
ET: Patient selection

• Inclusion criteria
  – Medication refractory
  – Functionally disabling in ADL (eating, drinking, writing)
  – Social stigma
  – Realistic expectations

• Exclusion criteria
  – Significant cognitive impairment
  – Relevant psychiatric comorbidity
  – Severe brain atrophy
  – Medical condition interfering with surgery or associated with limited life expectancy
Medical treatment

- Propranolol: 30–320 mg/d (↑↑)
- Primidone: 30–500 mg/d (↑↑)
- Combination: Propranolol + Primidone (↑↑)
- Topiramat: 400–800 mg/d (↑)
- Gabapentin: 1800–2400 mg/d (↑)
- Botulinum toxin for head tremor (↑)
- Botulinum toxin for voice tremor (↑)

Guidelines of German Society of Neurology 2015
DBS target for tremor

Munhoz et al 2016
Deep brain stimulation of the ventral intermediate nucleus in patients with essential tremor: Stimulation below intercommissural line is more efficient but equally effective as stimulation above

Michael T. Barbe a,b,*, Lena Liebhart a, Matthias Runge c, Janina Deyng c, Esther Florin a, Lars Wojtecki d,e, Alfons Schnitzler d,e, Niels Allert f, Volker Sturm c, Gereon R. Fink a,b, Mohammad Maarouf c, Lars Timmermann a,**

Tremor reduction:

• Comparison at same stimulation settings (p<0.01)
  – VIM Stimulation: 65%
  – PSA Stimulation: 86%

• Group comparison (n.s.) at individual stimulation settings
  – VIM Stimulation: 70% (mittl. Ampl. 5,73 Vc)
  – PSA Stimulation: 65% (mittl. Ampl. 3,51 Vc)

➡ PSA stimulation more efficient than VIM stimulation
➡ Same effect with VIM stimulation using higher stimulation amplitudes

N=19

Kinetic tremor

Postural tremor

Sydow et al. 2003
## ET: Comparison of treatments

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effective daily dosage</th>
<th>Estimated improvement in tremor amplitude</th>
<th>Recommendation according to EFNS criteria</th>
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</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td>60-240 mg</td>
<td>68%</td>
<td>A</td>
</tr>
<tr>
<td>Primidone</td>
<td>~ 150 mg</td>
<td>60%</td>
<td>A</td>
</tr>
<tr>
<td>Topiramate</td>
<td>100-333 mg</td>
<td>40%</td>
<td>B</td>
</tr>
<tr>
<td>Gapapentin</td>
<td>1200-1400 mg</td>
<td>39%</td>
<td>B</td>
</tr>
<tr>
<td>VIM-DBS</td>
<td>-</td>
<td>90%</td>
<td>B</td>
</tr>
</tbody>
</table>

Elble and Deuschl, MDJ 2011
Holmes tremor

- Rest, postural and action tremor
- Large, irregular amplitude, low frequency (<3–4 Hz)
- Often proximal upper extremities
- Medical treatment often unsatisfactory
- Occurrence weeks or years after causative lesion

Case reports and small series with thalamic DBS
- Overall improvement in tremor 76%
- Average age: 41 years
- Average follow-up of 3 years

- No specific patient selection criteria
Dystonic tremor

• Tremor occurring in a patient with dystonia
  – (1) associated dystonic posture
  – (2) irregular amplitudes and frequency (usually <7 Hz)
  – (3) postural/intentional tremor rather than resting tremor

• Tremor associated with dystonia
  – In a body part not affected by dystonia
  – Irregular, below 5 Hz.

• Case reports and small series of VIM DBS
  – Mixed but generally positive results
  – Gpi DBS seems less effective

  – No specific patient selection criteria
FXTAS

- Inherited, X-linked, adult-onset neurodegenerative disorder
- Caused by a expanded trinucleotide repeat IN fragile X mental retardation 1 (FMR1) gene.
- Occurs predominantly in men
- Action tremor, gait and limb ataxia
- Cognitive and neuropsychiatric dysfunction
- Parkinsonism, dysautonomia, and peripheral neuropathy

VIM stimulation in several patients with tremor improvement ranging from 30% to 70%
Multiple sclerosis associated tremor

- High prevalence of tremor in the MS population (25 to 58%)
- Most commonly postural tremor and/or intention tremor.
- Small case series and reports on thalamic stimulation:
  - Initial improvement tends to diminish beyond 1 year
  - Tremor reduction not readily associated with improvement in disability scores
  - Complication rate tends to be higher:
    - Perioperative seizures 8%
    - New neurological deficits 7%

- Prospective study, N=12
- Tremor and Quality of life
- After 2 und 12 Monate
- Results:
  - Significant tremor reduction after 2 and 12 months
  - Functional improvement only after 2 months
  - Functional health and well-being (SF-36) not improved
MS Tremor: recommendations for patient selection

• Only in very selected cases
• Tremor should be the main cause of disability
• Neurological deficits other than tremor must be considered
• Differentiate between tremor and ataxia (which typically does not respond)
• MS disease activity should be stable in last year
• Functional improvement is usually less than tremor reduction
Key points: Tremor

- DBS can be considered for patients who are severely affected by a medication refractory tremor.
- Virtually all types of tremor are eligible but sufficient evidence is only available for ET and PD tremor.
- ET and PD tremors are highly likely to improve whereas other tremor forms have a less favourable outcome.
- The target is the lateral thalamus (VIM nucleus) in almost all types of tremor except for PD tremor where the preferred targets is the STN.
- A bilateral procedure is usually preferable, especially in head, voice or trunk tremor.
Idiopathic generalized/segmental dystonia

  - 40% to 50% improvement after 3 months in sham-controlled, double-blind evaluations
- 50% to 60% improvement 3 years and
- 5 years after surgery (Volkmann et al, Lancet Neurol 2012)
- Younger age at time of surgery, shorter duration and less severe dystonia are correlated with better motor improvement (Witt et al, MDJ 2013)
Pallidal deep brain stimulation in patients with primary generalised or segmental dystonia: 5-year follow-up of a randomised trial

Jens Volkmann, Alexander Wolters, Andreas Kupsch, Jörg Müller, Andrea A Kühn, Gerd-Helge Schneider, Werner Poewe, Sascha Hering, Wilhelm Eisner, Jan-Uwe Müller, Günther Deuschl, Marcus O Pinsker, Inger-Marie Skogseid, Geir Ketil Roeste, Martin Krause, Volker Tronnier, Alfons Schnitzler, Jürgen Voges, Guido Nikkhah, Jan Vesper, Joseph Classen, Markus Naumann, Reiner Benecke, for the DBS study group for dystonia*
Cervical dystonia

• Class I randomised, sham-controlled trial: 26% reduction of CD severity and related disability (Volkmann et al, Lancet Neurol 2014)

• Four class III studies: N=32, F-U 12-60 months, 50% improvement in the TWSTRS (Kiss et al, Neurosurg Focus 2004; Pretto et al, J Neurosurg 2008; Skogseidet al Eur J Neurol 2012; Walsh et al, Brain 2013)

• Generally well-tolerated procedure
  – Dysarthria, transient neuropsychiatric symptoms
Secondary dystonia

- In general, less evidence for the effectiveness of DBS in secondary and neurodegenerative dystonias than for idiopathic focal generalized/segmental forms.
- Initial improvement often followed by worsening related to disease progression.
- Risk of side effects from DBS seems greater.
- Currently no specific and clear guidelines defining suitable patients with secondary dystonia.
Tardive dystonia

• Class II evidence for GPi-DBS (Pouclet-Courtemanche et al, Neurology 2016)
  – Severe pharmacoresistant TD (N=19)
  – Extrapyramidal Symptoms Rating Scale [ESRS]
  – Abnormal Involuntary Movement Scale [AIMS])
  – Cognitive scales, and a psychiatric assessment
  – Baseline, 3, 6, 12 months, 6-11 years (N=14)
GPi DBS in tardive dystonia

Pouclet-Courtemanche et al, Neurology 2016
GPi DBS in tardive dystonia

• Excellent cognitive and psychiatric tolerability of the procedure
• No cognitive decline
• Mood improved in most of the patients
Dystonia: Patient selection

- Primary segmental/generalized or cervical dystonia
- All types of dystonia can principally be considered
- Symptoms should be disabling enough
- Generalized/segmental dystonia: failure of anticholinergic drugs, benzodiazepines, and levodopa
- Cranial and cervical dystonia: failure of Btx
- In general, not mandatory to have tried all available medications
- No widely accepted consensus about which type of medication, which dose, or how many trials before surgery
- Dedicated multi-disciplinary movement disorder center
Dystonia: Patient selection

- Burke-Fahn-Marsden (BFMD) Dystonia Rating Scale
- Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)
- Quality of life (QoL) scales should be considered
- No agreement about which scales to use, or which threshold scores for disability, dystonia, and pain severity
Dystonia: Presurgical investigations

- Brain MRI scan
  - support the diagnosis of idiopathic or secondary dystonia
  - presence of minor structural abnormalities in the basal ganglia in idiopathic dystonia is not a contraindication for DBS

- Cervical spine MRI scan may be useful in cervical dystonia
  - to assess the degree of cervical spondylosis and any need for spinal surgery before or after DBS

- Skeletal imaging
  - to quantify spinal deformities that are common in children with DYT-1 dystonia

- Complete neuropsychology/psychiatric assessment
Segmental dystonia
Tardive dystonia
Thank you for your attention