Programming hyperkinetic patients (dystonia, tremor) with DBS

First programming and early follow-up

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1st Summer School on Neuromodulation for Movement Disorders
July 6-8 2017, Grenoble, France
It is important to tell the patient that

- The clinical benefit is generally not immediate and can require several months
- The benefit may be suboptimal and very variable (dystonia is a clinical syndrome!)
Post-operative Programming
Globus Pallidus pars interna (GPi) DBS (I)

- Often variable pallidotomy-like effect (pain and dystonia improvement), which can last for several weeks
  - Start the programming when the patient is close to the pre-operative condition (more reliable assessment)
  - Checking the electrodes localization and symmetry in the post-operative brain MRI may suggest potential side effects and help in programming the settings
  - Check the impedences
Both programming and management of the patients are performed with VCS.

As in PD, assessment of threshold for side effects contact by contact (130Hz/60micros), each lead separately

- Ventral (optic tract): flashes in controlateral visual hemifield are common with the lowest contacts
- Medial (internal capsule, corticobulbar fibers): controlateral face, hand contraction; dysarthria
- Inferior/ventral border : dizziness, nausea
- Lateral (GPe) : dystonia worsening
GPi: Effectively-Placed Bilateral Leads

Medtronic 3387 DBS leads shown in both hemispheres

<table>
<thead>
<tr>
<th>Anatomy</th>
<th>Preferred Location for DBS Lead</th>
<th>Observed Effect If Stimulated</th>
</tr>
</thead>
<tbody>
<tr>
<td>GPi</td>
<td>Posteroventral aspect of GPi</td>
<td>Reduction in parkinsonian or dystonia symptoms</td>
</tr>
</tbody>
</table>

Point to consider: The DBS lead may intentionally be placed slightly anterior or lateral in dystonia patients to allow for the use of higher voltages during programming.
GPI: Medial Observed Effects

<table>
<thead>
<tr>
<th>Anatomy</th>
<th>Location Relative To GPI</th>
<th>Observed Effect If Stimulated</th>
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</thead>
<tbody>
<tr>
<td>Posterior limb of internal capsule</td>
<td>Medial and posterior</td>
<td>Muscle contractions</td>
</tr>
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</table>
GPI: Ventral (Deep) Observed Effects

Left hemisphere, 3387 lead, unipolar contact 0
Putamen
GPe
GPI
Caudate nucleus
Optic tract
Optic chiasm
Stimulation spread into left optic tract

<table>
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<tr>
<th>Anatomy</th>
<th>Location Relative To GPI</th>
<th>Observed Effect If Stimulated</th>
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</thead>
<tbody>
<tr>
<td>Optic tract</td>
<td>Inferior</td>
<td>Phosphenes ('flashing lights') in contralateral visual hemifield</td>
</tr>
</tbody>
</table>
# GPI: Lateral Observed Effects

**Anatomy** | **Location Relative To GPI** | **Observed Effect If Stimulated**
---|---|---
GPe | Lateral and anterior | No effect (possible improvement in PD symptoms)
Putamen | Lateral and anterior to GPe | No effect

*Brain Orientation*

- **Left hemisphere, 3387 lead, unipolar contact 1**
- **Caudate nucleus**
- **Putamen**
- **GPe**
- **GPI**
- **Optic tract**

*Stimulation spread is primarily within GPe*
The time course of the clinical improvement is variable (from hours to weeks)

As first screening, we leave each contact in monopolar stimulation with a fixed voltage for one week (starting from 0 up to 3)

The best contact of stimulation (according to examiner and patient) will be tested at each side for a more prolonged time (1 month) at 60 micros and 130 Hz

The ventral contacts usually show the best improvement

Revaluation as out-patient, 4 groups of stimulation settings to test, follow-up according to patient’s need
If no clear or not satisfactory benefit

- Wider pulse widths for at least a month (120 and 210 micros) (Vercueil et al, 2007)
- Double monopolar stimulation (the two best contacts)
- Lower (60 Hz) or higher (185 Hz) frequencies (Kupsch et al, 2003; Moro et al, 2004; Tagliati et al, 2007; Moro et al, 2009)
- Bipolar stimulation
- Cycling stimulation
- Consider to implant new electrodes in GPi or STN

Post-operative Programming
GPi DBS (IV)
Figure 1: Postoperative Management Algorithm

- Select best contact according to effect and adverse effects
  - Effect at single contact
  - No effect at single contact
    - Discharge with the best contact
      - Test 2 adjacent contacts
        - try to reduce adverse effects
        - no effect
          - Change Frequency: 80, 180 Hz
          - Increase Pulse width: 90-450 µs
          - Bipolar settings
        - Individual adjustment
        - Re-evaluation 3 month
          - Individual adjustment

Kupsch et al, 2011
For different types of Dystonia

- No major differences in programming

**However**

- Secondary or heredogenerative dystonias might improve only with very selective parameters of stimulation
  - HD (Moro et al, 2004; Fasano et al, 2008)
  - Neuroancanthocytosis (Wihl et al, 2001; Guehl et al, 2007)

- Some primary dystonia patients have worsened (without evident reason, i.e., electrode malpositioning) (Vidailhet et al, 2005)
GPi DBS: Timing of improvement

Improvement

Hours/days  Months

Phasic movements/tremor

Pain

Tonic postures/movements
Effects of amplitude, frequency and pulse width on cervical dystonia

- 8 pts with idiopathic cervical dystonia and bilateral GPI DBS at 28.6 ± 19.2 (mean ± SD) months after surgery

- Ten settings, including a combination of a wide range of pulse widths, low and high frequencies and voltage, were administered in a randomized double blinded fashion

Clinical improvement (57% TWSTRS severity score) was significantly associated with high frequency (≥60 Hz) and high voltage. Stimulation at 130 Hz showed the best clinical improvement. Increasing PW (from 60 to 450 μs) did not result in a significant improvement

Moro et al, 2009
Progressive improvement in segmental dystonia
Progressive, rapid improvement in Idiopathic Segmental Dystonia
(Immediate post-op programming)
Tremor

- Virtually any kind of tremor (dystonic, parkinsonian, MS, post-traumatic, post-stroke) can be improved by Ventralis Intermedius (Vim) thalamic nucleus DBS
- Previous failure of all the available medical treatments
- Brain MRI
- (Neuropsychological assessment)
- Video Tremor Scale
Postoperative Programming

Vim DBS (I)

- Often evident thalamotomy-like effect, which can last several weeks
  - Better start the programming when the patient is close to the pre-operative condition for a more reliable assessment
  - Check MRI and impedences
- As in STN, assessment of the threshold for clinical benefit and side effects contact by contact (VCS, 130Hz/60micros)
- Useful to use a clinical parameter, such as drawing a spiral, writing a word, holding a cup
  - Paraesthesia, contraction and dysarthria are common side effects
Postoperative Programming
Vim DBS (II)

- It is not unusual to use a bipolar setting (less side effects) with
good clinical benefit

- The time course for the clinical improvement is immediate!

- ….but sometimes hours/days for SE (ataxia, dysarthria)

- Usually lowest contacts most effective for tremor control BUT also
more cerebellar SE!

- Mild tingling in the contralateral face and hand when initiating
stimulation is common, with an optimally placed lead
Vim DBS: Electrical Parameters of Stimulation

- **Limousin et al, Lancet 1991**
  - 4 PD pt with external stimulation some days after surgery
  - External stimulation (WPI)
  - Beneficial effect started ≥ 60 Hz, peaked from about 150 to 1000 Hz and then slowly fell until 5000 Hz

Relation between electrical stimulation frequency and intensity necessary to abolish tremor in four individual patients. Semi-log representation, fourth order polynomial regression curve.
**Vim DBS:**

**Electrical Parameters of Stimulation**

- **O’Suilleabhain et al, Neurology 2003**
  - 11 pt (7 ET, 4 PD)
  - Voltage was consistently predictive of tremor response
  - No significant difference between 130 and 185 Hz
  - 90 better than 60 micros
  - Monopolar better than bipolar

*Figure 2. Grand average voltage response curves for essential tremor (ET) (A, C, E) and PD (B, D, F) for bipolar (■) and monopolar (♦) configurations.*
Vim DBS Side effects

Spread of current:

- Ventral spread of current (dentate-thalamic fibers): Ataxia, dysmetria, cerebellar dysarthria
- Posterior (medial lemniscus): paresthesias, pain

The site of paresthesias may help to predict the mediolateral location of the electrode (somatotopy within the VIM: leg area is lateral, hand and face are medial)

- Lateral (internal capsule): dysarthria and contralateral tetanic contraction of the face, hand, and more rarely lower limb
- Non-localizing SE: mild hemineglect, dizziness and postural instability
Vim: Effectively-Placed Unilateral Lead

- Medtronic 3387 DBS lead shown in left hemisphere

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<tr>
<td>Vim</td>
<td>Middle of nucleus, DBS tip 1-2 mm anterior to VC border, contact 0 at base of Vim</td>
<td>Tremor arrest</td>
</tr>
</tbody>
</table>

Point to consider: The Vim nucleus is somatotopically organized along a medial-lateral axis. Face/tongue representation is medial, foot is lateral.
## Vim: Posterior Observed Effects

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<th>Observed Effect If Stimulated</th>
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<tbody>
<tr>
<td>Vc nucleus</td>
<td>Posterior</td>
<td>Paresthesias that increase in severity with increasing voltage</td>
</tr>
</tbody>
</table>

**Points to consider:** The Vc nucleus is somatotopically organized along a medial-lateral axis. Face/tongue representation is medial, foot is lateral. Transient paresthesias do not necessarily indicate a lead that is too posterior.
Anatomy | Location Relative To Vim | Observed Effect If Stimulated
--- | --- | ---
Posterior limb of internal capsule | Lateral | Dysarthria, facial pulling, muscle contractions

Point to consider: The internal capsule is somatotopically organized along an anterior-posterior axis. Face representation is anterior, foot is posterior.
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<th>Observed Effect If Stimulated</th>
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<tbody>
<tr>
<td>Brachium conjunctivum (cerebellar fibers)</td>
<td>Ventral and medial</td>
<td>Ataxia</td>
</tr>
<tr>
<td>Zona incerta</td>
<td>Ventral</td>
<td>No effect on tremor</td>
</tr>
<tr>
<td>Medial lemniscal pathway</td>
<td>Ventral and posterior</td>
<td>Paresthesias</td>
</tr>
<tr>
<td>Internal capsule</td>
<td>Ventral and lateral</td>
<td>Dysarthria, muscle contractions</td>
</tr>
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In case of similar results for 2 or more contacts, blind assessment(s) of the benefit may be useful to determine the hierarchy of contacts.

In patients with bilateral implantation, check the efficacy of one electrode at a time, turning OFF the other side.

In contrast, both sides should be ON when addressing the occurrence of side effects, as axial cerebellar signs (dysarthria, imbalance) are much more common with bilateral procedures.

Patients start chronic stimulation at the end of the initial programming with the minimal voltage that controls tremor without any acute side effects.
Postoperative Programming
Vim DBS (IV)

- After the first programming visit, patients come back for 1–2 appointments to optimize stimulation settings and verify the absence of stimulation-induced side effects.

- In case of poor tremor control:
  - Frequency can be increased [Dowsey-Limousin, 2002]
  - Other configurations of settings (i.e., double monopolar stimulation)
  - PW can be increased, although this is more likely to induce side effects due to the chronaxie properties of the axons reaching the thalamus
  - In case of side effects, bipolar stimulation can be considered.
The majority of ET patients complete the programming in less than 2 months.

Clinicians may set a given range of a parameter (typically voltage) and patients are instructed on how to slowly tune the stimulation at home with the help of the patient’s remote control.

Patients are also taught on how to switch the stimulation OFF at night (not in PD tremor) to save battery life and avoid tolerance to stimulation (loss of benefit) in the long-term.
Vim DBS for ET

L VIM-DBS
9 yrs post-op
STIM OFF
Acknowledgments: Grenoble DBS team

Pr. E. Moro
Dr. V. Fraix
Dr. A. Castrioto
Dr. S. Meoni
Pr. B. Debu

Pr. S. Chabardes
Dr. E. Seigneuret

A. Bichon
E. Lhomme
E. Schmitt
E. Chevrier
A. Kistner
P. Pelissier
Fellows, residents & students
THANK YOU!