Deep Brain Stimulation - DBS

Technological innovations

Alberto Priori

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INNOVATIVE FIELDS

Current steering (Pollo et al 2014, Barbe et al 2014)

Dual Stimulation (Sims William et al 2013)

Interleaving (Baumann et al 2012, Wojtecki et al 2011)

Coordinated reset–CR (Tass et al 2012)

aDBS (Priori et al 2012)

Web database (Rossi et al 2013)

Spatial Resolution

Time Resolution

Patient Personalization

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(Priori 2015)
STEERING STIMULATION

- **Current steering** based on new electrodes allowing directing the EF radially and longitudinally with multiple contacts

- Stimulating device allowing independent control different contacts

VERCISE (Boston Scientific)

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Steigerwald et al, Mov Disord 2016
La steering stimulation consente di avere una maggiore finestra terapeutica.
INTERLEAVING STIMULATION

- **Interleaving stimulation** → a pair of electrodes each delivering a different amount of charge pulses but at the same frequency
- For patients not responding to conventional DBS
- Tested in PD, ET and dystonia
- Limitation
  - Time consuming programming
  - Relatively short battery duration

*Miocinovic et al, Parkisonism Related Disorders 2014*
INTERLEAVING STIMULATION

Programming according to anatomical (electrode position) and clinical

Step 1: Patient has proven ineffective in PD or intolerable with side effects by conventional programming.

Step 2: Perform standard algorithm: 1. Perform monopolar review of all contacts individually (set pulse width at 60 µs and rate at 130 Hz). 2. Increase amplitude gradually to define the functionality and threshold for side effects of each contact.

Step 3: 1. Refer to each patient’s symptoms and reconstruction images. 2. Choose most suitable contacts according to the result from step 2.

Step 4: 1. Select most effective contacts (according to step 3) as one program (ILS1) which have satisfactory motor benefit and limited side effects. 2. Increase ILS1 amplitude and pulse width gradually to achieve maximum motor benefit below the threshold of adverse effects.

Step 5: ILS2 use other contacts (according to step 3) and increase amplitude and pulse width gradually to further improve PD or avoid side effects.

Step 6: Additionally, 1. Use bipolar mode to decrease side effects. 2. Use low frequency and contacts near the substantia nigra pars (usually lower contacts) as ILS2 to improve gait disturbance. 3. Use low frequency to alleviate dysarthria. 4. Decrease stimulation intensity (amplitude, pulse width) to avoid dyskinesias.

Zhang et al, 2016

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DUAL STIMULATION

• Delivered through a single 16-contacts electrode independently stimulating two structures

• Electrodes with more than 4 contacts which can be independently controlled

Figure 2. Dual frequency stimulation using a single electrode technique to target the Periaqueductal Grey/Periventricular Grey (PAG/PVG) and Centromedian Intralaminar Parafascicular complex (CMPf) in the treatment of chronic pain. (a) Tracings of the CMPf (blue) and PAG/PVG (red) in coronal plane undergo volumetric reconstruction using Neurolink™ software to create 3-dimensional structures for robot-guided DBS electrode implantation; (b) Contacts 1-3 and 5-8 are embedded within the PAG/PVG and CMPf respectively along the same trajectory; (c) Spherical electrical fields (red) at contacts 4 and 8 stimulate the PAG/PVG and CMPf respectively yielding analgesia in a case of refractory phantom limb pain.

Hollingworth et al, Brain Sci, 2017
ADAPTIVE DBS o CLOSED LOOP DBS

The choice of the control variable is crucial.

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POSSIBLE CONTROL VARIABLES

- Are adjunctive implants necessary?
- Are changes in surgical procedure required?
- Is the new device/implant well tolerated by the patient?
- Do control variables correlate with the clinical state?
- Can the system be personalised to the specific clinical phenotype?
- Does the system decrease battery duration?
- Is there any proof-of-concept?

(Arlotti 2016)

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<table>
<thead>
<tr>
<th>CONTROL VARIABLES</th>
<th>sEMG and accelerometers</th>
<th>Cortical neurosignals</th>
<th>Basal ganglia LFPs</th>
<th>Neurotransmitters</th>
</tr>
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<tbody>
<tr>
<td><strong>Additional implant/equipment</strong></td>
<td>YES – external sensors required</td>
<td>YES – implanted cortical electrodes required</td>
<td>NO – LFPs are recorded from the implanted DBS electrode</td>
<td>YES – at least 4 additional CFMs</td>
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<td><strong>Changes in the surgical procedures</strong></td>
<td>NO – the additional implant is external and does not affect the surgical procedure</td>
<td>YES – the surgery needs to include the implant of cortical electrodes</td>
<td>NO – no additional implant during surgery</td>
<td>YES – the additional CFMs need to be implanted during surgery</td>
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<td><strong>Patient’s management/acceptability</strong></td>
<td>NO – it may be difficult to manage the recording sensors and the external equipment may be uncomfortable</td>
<td>YES – all the equipment is implanted</td>
<td>YES – the patient perceives the same system as for traditional DBS</td>
<td>NO - CFMs have a time life of only a few months and have to be replaced</td>
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<tr>
<td><strong>Correlation with the clinical state</strong></td>
<td>YES/NO – optimal correlation with tremor, but no correlations with rigidity and bradikinesia</td>
<td>YES – EcoG phase amplitude coupling and M1 action potentials correlate with main PD symptoms and can be used to drive aDBS</td>
<td>YES – multiple LFP oscillations are modulated by levodopa administration, DBS, movements, and non-motor tasks even years after electrode implant</td>
<td>YES - the time duration of tremor-free period is comparable to the duration of increased levels of stimulation-induced dopamine release after DBS pulse trains</td>
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<td><strong>Personalization and adaptability</strong></td>
<td>NO – cannot be used if patients do not show tremor</td>
<td>YES/NO – it may encode patient specific information</td>
<td>YES – the presence of multiple rhythms correlating with different patient’s characteristics may account for inter-subject variability</td>
<td>NOT YET TESTED</td>
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<td><strong>Low battery consumption</strong></td>
<td>YES/NO – the processing can be done externally, but triggers should be sent via telemetry links</td>
<td>YES/NO – the IPG needs to include the sensing circuit and the feedback algorithm</td>
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<td><strong>Proof of concept</strong></td>
<td>YES in humans (ET) [Yamamoto et al., 2013]</td>
<td>YES in animals [Rosin et al., 2011]</td>
<td>YES in humans (PD) [Little et al., 2013; Rosa et al., 2015; Little et al., 2015]</td>
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ACCELEROMETRY & EMG

Tremor onset prediction in 4 PD patients (Basu et al. 2013):
100% sensitivity
80% accuracy


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ACCELEROMETRY

(Cagnan et al. 2017)

PATIENTS WITH ET

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# ACCELEROMETRY

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CORTICAL BIOPOTENTIAL

- Single and Multi-unit activity based on micro-electrode arrays (MEA)
- Electrocorticography (ECoG)
- Surface electroencephalography (sEEG)

(Hemptonne et al.2015)

(Rosin et al.2011)

(Herron et al.2015)
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### Cortical Neurosignals

- **YES** – it may encode patient specific information
- **YES/NO** – the IPG needs to include the sensing circuit and the feedback algorithm
- **YES in animals [Rosin et al., 2011]**

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NEUROCHEMICAL SIGNALS

(Dopamine concentration changes with closed loop DBS) (Chang SY et al. 2013; Graham et al. 2014)
**NEUROCHEMICAL SIGNALS**

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LOCAL FIELD POTENTIALS (LFPs)

DEEP EEG ACTIVITY

Local field potential

DBS electrode

Neuronal population

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LOCAL FIELD POTENTIALS

LFPs CAN BE CAPTURED BY THE SAME ELECTRODE DELIVERING DBS

1. No additional implant
2. No changes in surgical procedure
3. Acceptable by the patients as conventional DBS

An electronic device for artefact suppression in human local field potential recordings during deep brain stimulation

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Rossi et al. 2007
LFPs correlate with the clinical state

*Risposta alla terapia dopaminergica*

(Priori et al 2004)
LFPs correlate with the clinical state

Risposta al movimento volontario

Correlazione a rigidità e bradicinesia

(Foffani et al 2005)

(Kuhn et al 2009)

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LFPs correlate with the clinical state

Dyskinesias

(A Alonso-French et al 2006)

(Foffani et al, 2005)

(Rodriguez-Oroz et al 2011)

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LFPs correlate with the clinical state

Response to DBS

(Quinn et al, 2015)
aDBS IN HUMANS: APPROACH 1

Voltage modulation of stimulation in function of the STN beta power

Rosa et al. 2015 e 2017
Arlotti et al, 2017

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aDBS IN HUMANS: APPROACH 2

Off/on DBS in function of a given beta power level

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Little et al. 2013

Little et al. 2015
COORDINATED-RESET DBS

- train of high frequency through electrodes different from those implanted
- Tested in primate and humans → beta reduction and clinical improvement

Adamcich et al, Mov Disord, 2014

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