Treatments for patients with disorders of consciousness

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Introduction

Mesocircuit fronto-parietal model

Drugs | DBS | tDCS | Conclusion

Amantadine

Dopaminergic agent (Parkinson)


Schnakers et al, JNNP, 2008

n=184
Zolpidem

Short-acting nonbenzodiazepine GABA-A agonist hypnotic

1/15 responders  
= 6.7%  
*Whyte & Meyers, 2009*

4/84 responders  
= 5%  
*Whyte et al, 2014*

4/60 responders  
= 6.7% no change of diagnosis  
*Thonnard & Gosseries et al, 2014*

Drugs | DBS | tDCS | Conclusion

Chatelle & Thibaut, et al., *Front Hum Neurosci*, 2014
Deep brain stimulation

Intralaminar nuclei stimulation induces “recovery” from minimally responsive state

Deep brain stimulation

Clinical improvement

| Intelligible Words | 3 |
| Vocalization Only  | 2 |
| Sustained Attention| 3 |
| Eyes Open w/o Stim | 2 |
| Eyes Open w/ Stim  | 1 |
| Functional Object Use | 6 |
| Automatic Movement  | 5 |
| Object Manipulation | 4 |

DBS OFF  DBS ON

Verbal

Arousal

Motor

<table>
<thead>
<tr>
<th>Stimulation</th>
<th>Population</th>
<th>Effects</th>
<th>Authors</th>
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<td></td>
<td>Hemiplegic patients</td>
<td>Dexterity and strength</td>
<td>Hummel et al. Lancet, 2006</td>
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<td>Spastic patients</td>
<td>Spasticity &amp; ADL (activity of daily life)</td>
<td>Wu et al., Arch Phys Med Rehabil 2012</td>
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<td>Alzheimer’s patients</td>
<td>Memory</td>
<td>Ferrucci et al. Neurology, 2008</td>
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<td></td>
<td>Aphasic patients</td>
<td>Language</td>
<td>Baker et al. Stroke, 2010</td>
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</tbody>
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➡️ Cheap, easy to use & no severe side-effects

Thibaut et al, Rev Neurol, 2013

www.comascience.org
tDCS single session

- Randomized, double blind, sham controlled, cross-over study
- Direct current; 2 mA; 20 min
- 55 patients included (25 VS/UWS; 30 MCS; 35 chronic; 25 TBI; 43±18y)

Thibaut et al., Neurology, 2014
tDCS single session

Treatment effect: delta CRS-R total scores

**Delta CRS-R total score** (median – IQR – min-max)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Delta CRS-R Total Score</th>
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<td><strong>MCS</strong> (n=30)</td>
<td><img src="MCS_graph.png" alt="Graph" /></td>
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<tr>
<td><strong>VS/UWS</strong> (n=25)</td>
<td><img src="VSUWS_graph.png" alt="Graph" /></td>
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* p<0.05

\[\text{Thibaut et al., Neurology, 2014}\]
tDCS single session

- **15/55 responders**: sign of consciousness after tDCS and not before tDCS or before and after sham
  - 2 VS/UWS; acute
  - 13 MCS (5 patients >1y post insult)

- Change of diagnosis
  - 3 MCS ➔ EMCS (acute)
  - 2 VS/UWS ➔ MCS (acute)

- No effect of time since injury or etiology
- No side effects

Thibaut et al., Neurology, 2014
Neural correlates

Can functional brain activity & grey matter atrophy predict tDCS clinical response?

- Data from study 1 – chronic MCS (n=24)
- FDG-PET – MRI (VBM)
- 8 tDCS responders (4 TBI, mean age: 38±19y)
- 13 tDCS non-responders (8 TBI, mean age: 36±14y)

Thibaut & Di Perri et al., under review

www.comascience.org
Neural correlates

- hypometabolic
- preserved
- p<0.05

PFDL cortex, precuneus, thalamus also more atrophic in non-resp.

Thibaut & Di Perri et al., under review
Repeated stimulations

Single stimulation: effects ± 60 min\(^1\) ➔ short-lasting improvements, back to initial state
1. Increase the duration of the effects
2. Increase the number of responders

Randomized sham controlled double blind cross-over

16 patients included in chronic MCS (12TBI; mean age 47±16y)

\(^1\)Nitsche et al., 2001
Thibaut et al., submitted
Repeated stimulations

Treatment effect: day 5 & day 12 – 53% of responders

Delta CRS-R total score (median – IQR – min-max)

-7 -6 -5 -4 -3 -2 -1 0 1 2 3 4 5 6 7

real sham

day 5

* p<0.05

Drugs | DBS | tDCS 3 | Conclusion

Thibaut et al., submitted
Repeated stimulations

- Longitudinal analysis:
  - Real session: significant + time evolution $(p<0.001)$
  - Sham session: no evolution across time $(p=0.64)$
Conclusion


Drugs | DBS | tDCS | Conclusion
THANK YOU