Source localization of the P300 event-related potential as a biomarker for the efficacy of vagus nerve stimulation in patients with epilepsy

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Introduction

- 50 million epileptic patients worldwide
- ± 33% not responsive to medication

Vagus Nervus Stimulation (VNS) is efficient alternative treatment for some patients [1]:

<table>
<thead>
<tr>
<th># patients</th>
<th>seizure reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responders (R)</td>
<td>1/3 &gt; 50%</td>
</tr>
<tr>
<td>Non-responders (NR)</td>
<td>1/3 30 – 50%</td>
</tr>
<tr>
<td>Non-responders (NR)</td>
<td>1/3 &lt; 30%</td>
</tr>
</tbody>
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Problem:
- Working mechanism unknown
- Unable to predict whether patient will benefit from VNS treatment or not before expensive and risky implantation

Goal: Investigate whether EEG source reconstruction can provide information on the working mechanism of VNS and whether a biomarker for the efficacy of VNS can be found

Data

P300 component modulated by norepinephrine level in the brain, which is linked to the anti-epileptic effect of VNS [2].

20 VNS patients performed auditory oddball task recorded with 60-channel EEG (Micromed System Plus, Mogliano Veneto, Italy) [3]

Main effect of group

What is the difference in brain activity between R and NR, independent of VNS OFF or ON?

R > NR
- Priors set 2:
  - p=6.9e-6
  - 297 voxels
- Priors set 3:
  - p=1.0e-5
  - 293 voxels

Mainly situated in the left hippocampus

NR > R
- Priors set 2:
  - p=6.1e-5
  - 195 voxels
- Priors set 3:
  - p=2.0e-4
  - 153 voxels

Mainly situated in the left insula

Main effect of VNS

What is the difference in brain activity when VNS is applied or not, independent of the patient being R or NR?

ON > OFF
- Priors set 2:
  - Pₚmax = 0.024
  - 238 voxels
- Priors set 3:
  - Pₚmax = 0.018
  - 427 voxels

Mainly situated in right hippocampus + amygdala

OFF > ON
- Priors set 2:
  - Pₚmax = 0.029
  - 70 voxels
- Priors set 3:
  - Pₚmax = 0.017
  - 422 voxels

Mainly situated in left amygdala and hippocampus [6]

Interaction group x VNS

What is the difference between R and NR when looking at the difference in both groups for VNS OFF and ON?

RₚON>RₚOFF
- Priors set 2:
  - Pₚmax = 0.0009
  - 300 voxels

No significant clusters

NRₚON>NₚOFF > RₚON>RₚOFF
- Priors set 3:
  - Pₚmax = 0.038
  - 27 voxels

Indication right hippocampus

Conclusion

Priors should be chosen large enough to find significant overlapping brain activity due to intersubject variability.

Significant differences in brain activity for responders vs. non-responders were found, indicating a possible biomarker for the efficacy of VNS.

Significant differences in brain activity were also found for VNS off vs on, providing information on the working mechanism of VNS.

The group x VNS test can serve as a biomarker for VNS and provides insights on the working mechanism of VNS, but the significance of the tests should be increased (more subjects, even larger priors, ...).

Although more research is needed, we showed the potential of EEG source reconstruction in the research on VNS.

References