Seizure freedom: The importance of structure-function coupling

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Introduction

Epilepsy is a common neurological disorder consisting of seizures, which can cause loss of consciousness and convulsions.
- One-third of epilepsy patients are inadequately treated by medication, in which case brain surgery may help prevent seizures.
- Unfortunately, up to half of patients may still have seizures post-surgery; better understanding of how different two group’s means are.

Aims
- We aim to extend research on structure-function coupling within epilepsy, by relating it to surgical outcome.
  - Hypothesis: the most harmful connections to patients will be the most strongly coupled, as these will be the most ‘epileptogenic’ connections.
  - Structure-function coupling will be strongest in the surgically removed brain connections of good outcome patients (rather than bad outcome), as the surgeon would be breaking the brain connections promoting the epilepsy.

Methods
- 23 patients → 10 = seizure-free post-surgery (good outcome), 13 = seizures/seizure symptoms persist post-surgery (bad outcome).
- Structural connectivity derived from white-matter tractography (aka neural nerve tracts).
- Functional connectivity inferred from neural electromagnetic recordings.
  - Diffusion-weighted magnetic resonance imaging (DW-MRI) and magnetoencephalography (MEG) data collected from UCL Hospital NHS Trust, and used to quantify structural and functional connectivity respectively.
  - Used 5 DW-MRI measures: length of neural connections, FA, QA, MD, and gFA connection insulation).
- Predominantly used one MEG oscillation frequency: Alpha.
  - Matrices for DW-MRI and MEG data created by Dr. Peter Taylor and Dr. Sriharsha Ramaraju respectively (see figure 1).
- Correlation taken between DW-MRI measures and MEG (see figure 2a and 2b). Mann-Whitney test used to determine differences between correlations for both outcome types (see figure 2c).

Results
- The below headings quantify the importance of our findings:
  - P-value → less than 0.05 indicates 95% certainty that the result did not occur by chance.
  - AUC closer to 0 or 1 indicates separation between groups (0.5 indicates no separation).
  - Table 1 shows structure-function coupling (between gFA and Alpha) can differentiate between surgical outcomes.
    - This result is depicted in figure 2(c) where you can see the correlations are strongest in good outcome patients.
    - These results can be reproduced using other structural measures, including FA and QA (see figure 3).

Table 1. P-value, AUC, and Cohen’s d of the correlation between structural connectivity measures and MEG (using alpha wave).

<table>
<thead>
<tr>
<th>Structural measure</th>
<th>P-Value</th>
<th>AUC</th>
<th>Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length</td>
<td>0.877</td>
<td>0.477</td>
<td>-0.235</td>
</tr>
<tr>
<td>FA</td>
<td>0.014*</td>
<td>0.192</td>
<td>-1.269</td>
</tr>
<tr>
<td>QA</td>
<td>0.017*</td>
<td>0.200</td>
<td>-1.194</td>
</tr>
<tr>
<td>MD</td>
<td>0.556</td>
<td>0.432</td>
<td>-0.199</td>
</tr>
<tr>
<td>GFA</td>
<td>0.008*</td>
<td>0.169</td>
<td>-1.156</td>
</tr>
</tbody>
</table>

Significant results indicated with an asterisk (*).

Discussion
- We are currently furthering these results by investigating seizure characteristics (focal vs. generalised seizures) rather than patient outcome.

Conclusions
- Structure-function coupling between gFA and Alpha frequency may be a marker of epileptogenic connections.
  - Structure-function coupling is significantly stronger in the surgically removed connections of good outcome patients, than bad outcome patients.
  - This result is strongest in gFA, but can be reproduced with other structural measures.
  - With further evidence, clinicians may choose structure-function coupling to inform surgery resection.
    - E.g. A surgeon may measure where the strongest gFA-Alpha coupling is, and choose to resect these connections to maximise the likelihood of seizure freedom.

References

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