Seizure freedom: The importance of structure-function coupling

| Ruby Scarlett*, 170071835, r.scarlett@newcastle.ac.uk |
| BSc Psychology | School of Medical Sciences | Supervisor: Dr. Peter Taylor |

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 which brain connections to remove may improve surgical outcomes.
- Structural connectivity = physical connections between brain areas.
- Functional connectivity = brain areas firing together.
  - 'Structure-function coupling' = a link between structural connectivity and functional connectivity (Shah et al., 2019).

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 (≈ neural connection insulation).
  - Predominantly used one MEG oscillation frequency: Alpha.
- Method of identifying surgery affected connections adopted from Taylor et al (2018).
  - 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).

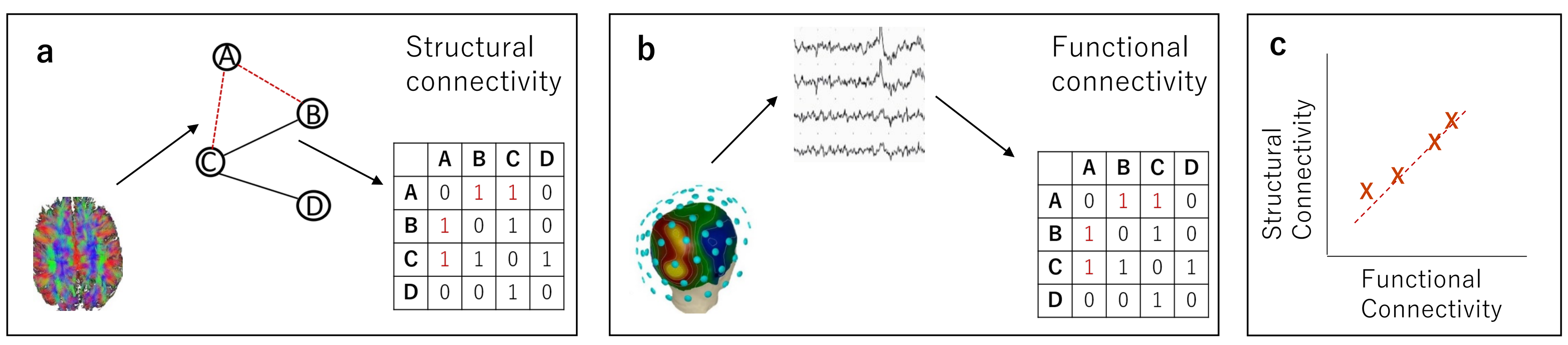

Figure 1. Creating a structural connectivity matrix from DW-MRI (a), and a functional connectivity matrix MEG (b). Finding the correlation (c) between the two.
Note: Non-zero elements indicate a connection. --- = surgically removed connections.

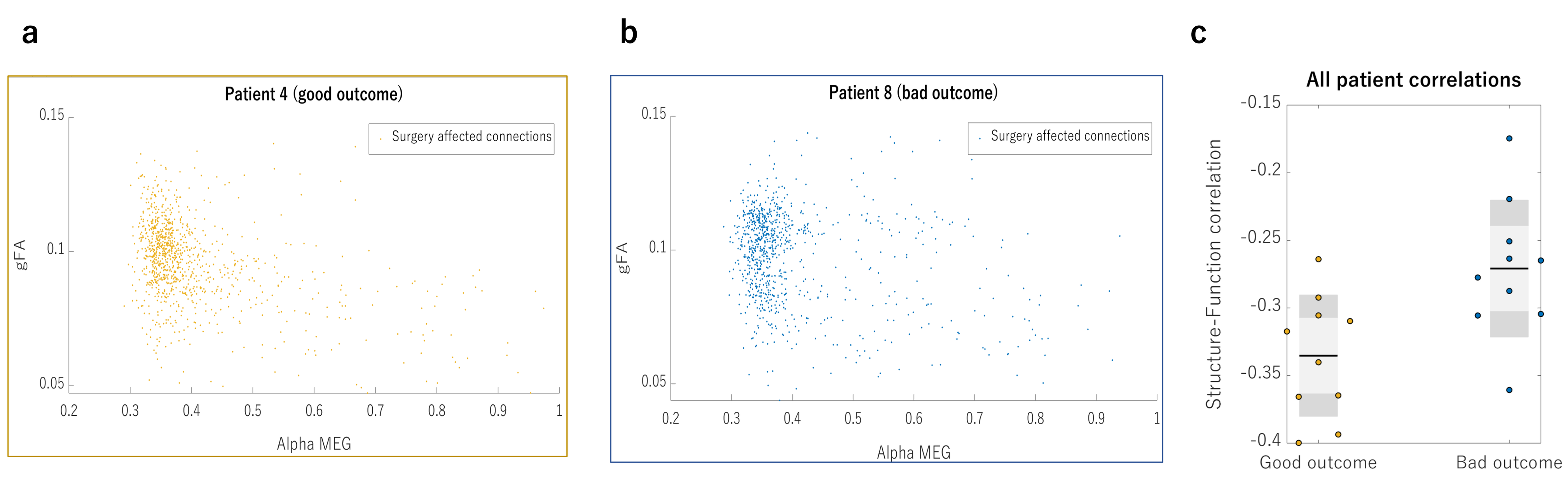

Figure 2. Structure-function (gFA-Alpha) correlations of patient 4 (a) and 8 (b), and the difference between all patient correlations sorted by outcome (c).

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).
  - Cohen's d → measures (in standard deviations) how different two group's means are.
- 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).

Structural measure	P-Value	AUC	Cohen's d
Length	0.877	0.477	-0.235
FA	0.014*	0.192	-1.269
QA	0.017*	0.200	-1.194
MD	0.556	0.432	-0.199
GFA	0.008*	0.169	-1.156

Significant results indicated with an asterisk (*).

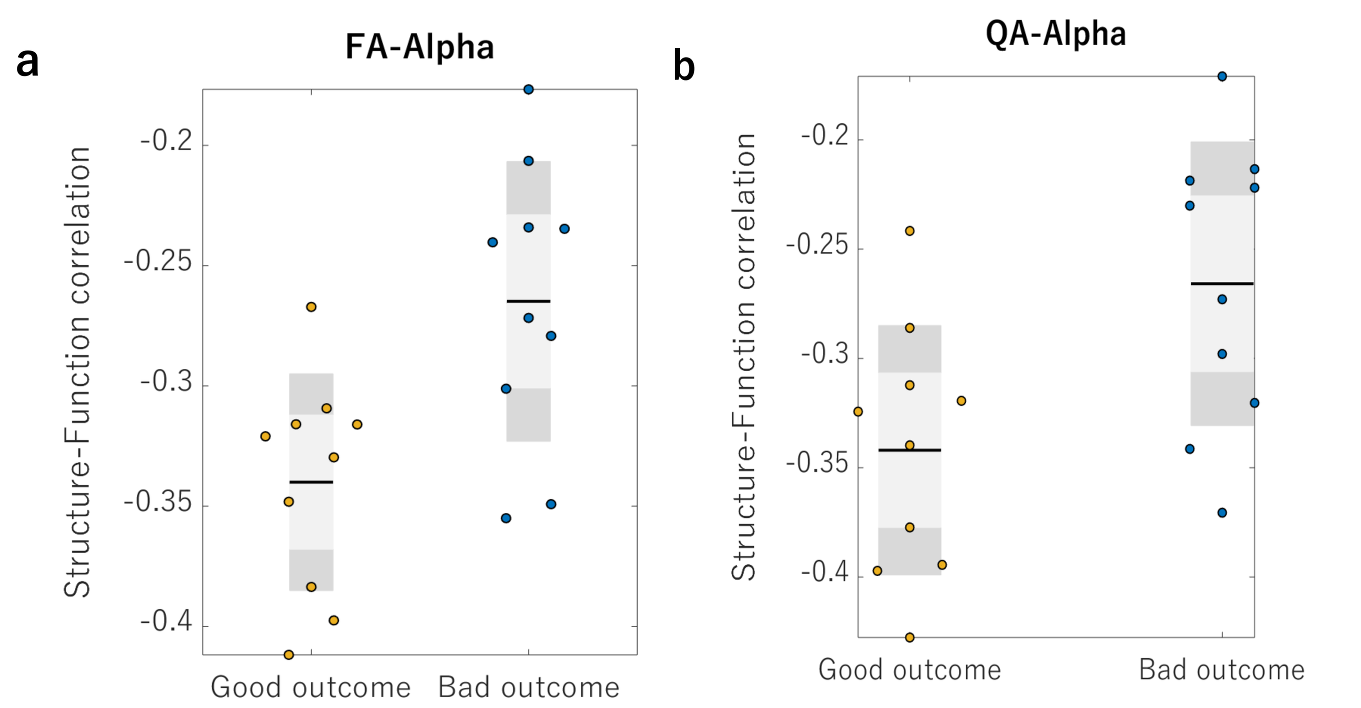

Figure 3. Examples of reproducibility, using FA (a) and QA (b) as structural connectivity, and alpha wave MEG as the functional connectivity.

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

Shah, P., Ashourvan, A., Mikhail, F., Pines, A., Kini, L., Oechsel, K., … & Litt, B. (2019). Characterizing the role of the structural connectome in seizure dynamics. *Brain*. 142(7), 1955-1972. https://doi.org/10.1093/brain/awz125
Taylor, P. N., Sinha, N., Wang, Y., Vos, S. B., de Tisi, J., Miserocchi, A., ⋯ Duncan, J. S. (2018). The impact of epilepsy surgery on the structural connectome and its relation to outcome. NeuroImage: Clinical, 18, 202–214. https://doi.org/10.1016/j.nicl.2018.01.028

Acknowledgments

Dr. Peter Taylor → Thank you for this opportunity and the guidance you've given me throughout the project.
UCL NHS Trust → Thank you for the data that has enabled this project and much other research.
Vacation scholarships → Thank you for funding for this project.