Measuring effective connectivity in resting-state MEG using PDC: Effect of ageing in the Cam-CAN project

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Background

There is growing interest in the networks of activity in the human brain at rest, eg. in terms of graph-theoretic properties that distinguish normal from pathological brain states. Such resting-state networks (RSNs) are often defined from *f*MRI, but this methodology cannot detect coherent activity above ~0.1Hz. Magnetoencephalography (MEG), on the other hand, can detect coherent networks at much higher frequencies, but is subject to a number of technical challenges.

First, the signal is contaminated with artifacts of both environmental and biological origin. Second, the spread of the magnetic field as it travels from the cortex to MEG sensors results in spurious dependencies between sensors. Third, finding a statistically significant level of connectivity using surrogate data is computationally infeasible.

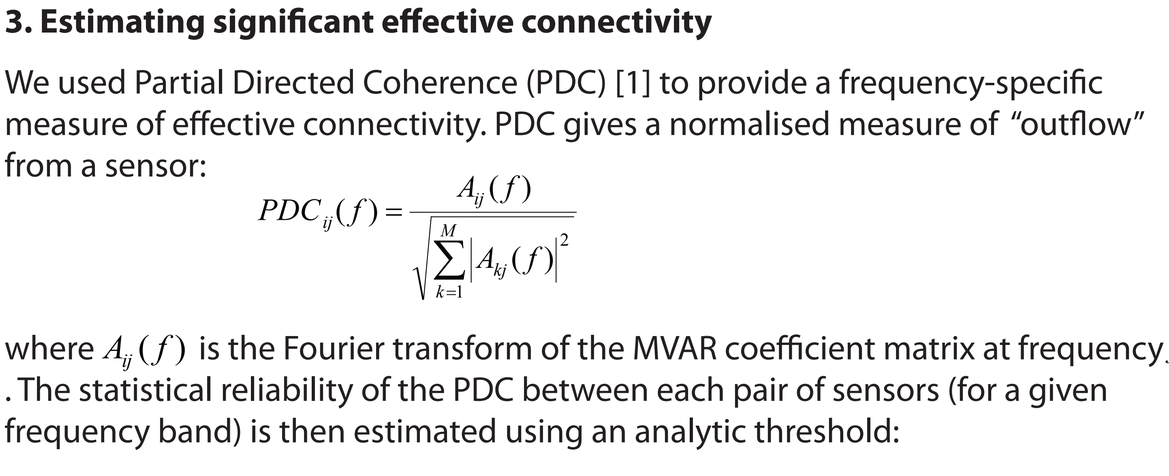
Here, we describe an MEG analysis pipeline that overcomes these problems, using multivariate autoregressive modelling to characterise time-lagged, directed dependencies between sensors. We demonstrate the use of this pipeline to detect differences in graph-theoretic properties of RSNs in young and older participants.

Methods

1. Pre-processing to remove noise

Signal Space Separation (SSS) is used to remove environmental noise. A spherical harmonic decomposition allows the magnetic fields arising within the sphere enclosed by the hemispherical MEG sensor-array (which include brain signals) to be separated from those arising from outside the sphere (which reflect environmental noise). This decomposition is also used to transform sensor-data from each subject to a standard head position, thereby obviating the need to solve the ill-posed problem of projecting the data to source space.

To remove artifacts of biological origin arising from within the sensor-array, Independent Component Analysis (ICA) is used to maximise the statistical independence between temporal components. Bootstrapping is then used to identify components that correlate significantly with the data recorded by ocular (EOG) and cardiac (ECG) electrodes, and these are projected out of MEG data.



2. MultiVariate AutoRegressive Modelling (MVAR)

The pre-processed data are modeled as a MVAR process:

$$x_i(t) = \sum_{j=1}^{M}\sum_{k=1}^{p} a_{i,j}(k)x_j(t-k) + u_i(t) \qquad i = 1,\ldots,M$$

where $x_i(t)$ are the time series for each of the M sensors, k is the time lag (up to model order p), $a_{i,j}$ are the model parameters to be estimated and $u_i(t)$ is assumed to be white noise. Information criteria are used to define the model order and the model assumptions are validated. Note that, because the MVAR measures time-lagged dependencies between sensors (k>=1), these dependencies cannot be an artifact of magnetic field spread, which would be instantaneous (k=0).

3. Estimating significant effective connectivity

We used Partial Directed Coherence (PDC) [1] to provide a frequency-specific measure of effective connectivity. PDC gives a normalised measure of "outflow" from a sensor:

$$PDC_{ij}(f) = \frac{A_{ij}(f)}{\sqrt{\sum_{k=1}^{M}\left|A_{kj}(f)\right|^2}}$$

where $A_{ij}(f)$ is the Fourier transform of the MVAR coefficient matrix at frequency f. The statistical reliability of the PDC between each pair of sensors (for a given frequency band) is then estimated using an analytic threshold:

$$PDCthresh_{ij}(f) = \sqrt{\frac{C_{ii}(f)\chi^2_{1,1-\alpha}}{T\sum_{k}\left|\hat{A}_{kj}(f)\right|^2}} \qquad C_{ij}(f) = Cov_{ii}[\sum_{k,l=1}^{p} H_{jj}(\cos(kf)\cos(lf) + \sin(kf)\sin(lf))]$$

where H is the inverse of covariance matrix of the MVAR process and T is the number of samples. Here, we use a Bonferroni-corrected threshold of α=0.05/(M*(M-1)).

Methods cont'd

Network analysis

After thresholding, the resulting binary graphs of PDC matrices can be characterised using graph-theoretic measures. Global network measures include:

1. Mean-degree 2. Mean clustering-coefficient 3. Global efficiency

Local measures for each sensor include:

1. Degree 2. Clustering coefficient 3. Local efficiency

Since these measures abstract away from type of data, they can be compared to those measured for RSNs of other neuro-imaging modalities, such as *f*MRI, or to those derived from simulations of network change, eg. in ageing.

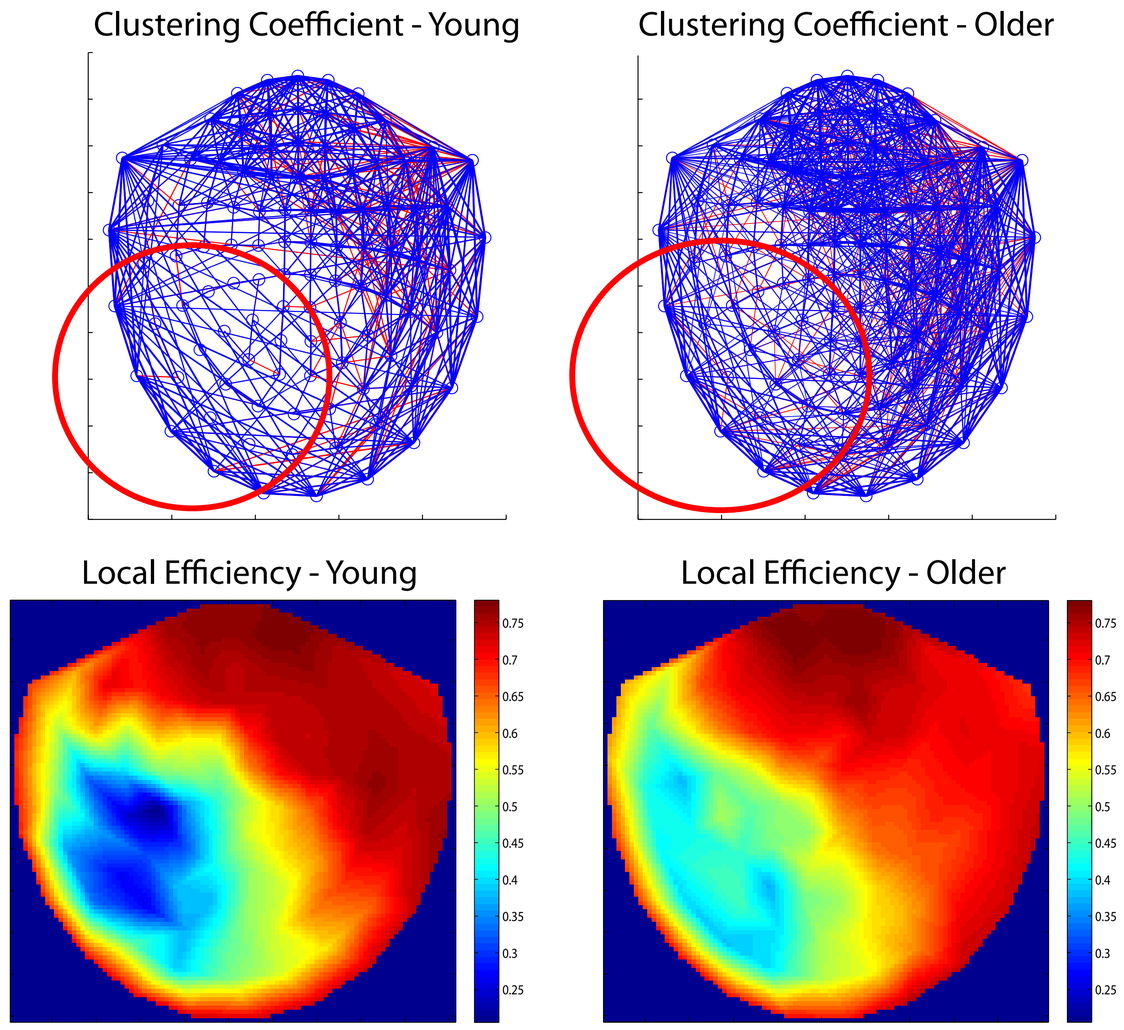
Data

We applied the method to 8.5 min of resting-state data sampled at 1 kHz from 204 planar gradiometers in 24 young (18-38) and 24 older (68-88) subjects. These data are part of the Cam-CAN project (www.cam-can.org), which will eventually have datasets from 700 people between 18 to 88 years of age. *t*-tests were used to compare network measures for young versus older participants, with Random Field Theory (RFT) being used to correct for multiple comparisons on local network measures. While binary PDC matrices were calculated for 6 common frequency bands, we present results here for just the delta band (1-4 Hz).

Results

The young and older group did not differ significantly in terms of model order (so a fixed value of *P*=23 was used below), model fit, or mean autoregressive parameters. Nor did they differ in their global network properties.

For the local network measures however, there was a cluster of left parietal sensors that showed a higher clustering coefficient and higher local effiiciency for older than younger groups (correcting for multiple comparisons across sensors).



Conclusion

This work describes a novel pipeline for estimating resting-state networks of significant effective connectivity between MEG (or EEG) sensors. The pipeline was used to reveal an effect of age on the network metrics of clustering coefficient and efficiency over left parietal sensors.

Future work will explore these age effects parametrically in the larger Cam-CAN sample, and relate them to the same measures on resting-state *f*MRI data from the same sample and to simulations of how ageing might affect functional interactions between brain regions.

References

1. **Baccala, L. A. & Sameshima, K.** (2001) Partial directed coherence: a new concept in neural structure determination. *Biol. Cybern.* 84, 463-474
2. **Schelter, B., Winterhalder, M., Eichler, M., Peifer, M., Hellwig, B., Guschlbauer, B.** (2006) Testing for directed influences among neural signals using partial directed coherence. *J Neurosci Methods* 152:210-219