Network-based statistics for longitudinal (unbalanced) samples: NBR, an R package

Zeus Gracia-Tabuenca & Sarael Alcauter
Instituto de Neurobiología, Universidad Nacional Autónoma de México

The connectome models the brain as a set of interacting elements, allowing to characterize the brain from a systems perspective using network science. In particular, Zalesky et al. (2010) proposed Network-based Statistics (NBS) a mathematical approach that allows statistical inferences at the (sub-)network level, with a trade-off between false positive control and higher statistical power than mass univariate approaches (e.g. FDR). Nevertheless, NBS is based on general linear hypothesis testing (GLHT) which potentially limits its application to longitudinal samples, particularly, with an unbalanced sample, i.e., with a variable number of sessions per subject. We implemented a publicly available R software package, NBR (Network-Based R-statistics), that performs linear mixed-effects models (LME) in the NBS framework, allowing the exploration of unbalanced longitudinal samples.

We tested GLHT- and LME-NBS in the public dataset INDI-SLIM, which includes 333 participants (145 males; 17-28 y.o.) with two (n=212) or three (n=121) sessions each. All sessions include a resting-state fMRI scan and psychometric data. State anxiety scores and connectivity matrices between brain lobes were extracted. GLHT and LME tested the edgewise brain-behavior relationship for balanced (424 matrices) and unbalanced (787 matrices) samples, respectively.

The LME approach found a significant subnetwork associated with state anxiety, which includes the cingulum, frontal, parietal, occipital, and cerebellum (pFWE = 0.001), while GLHT found no significant results (pFWE = 0.355).

In summary, we developed an R package that implements LME for NBS. We showed that LME-NBS overpowers GLHT-NBS when dealing with unbalanced longitudinal samples. This is important given that missing data is very common in longitudinal samples, and balanced testing could dramatically undermine statistical power. Hence, considering the growth of longitudinal samples in neuroscience, we anticipate this method being potentially useful in the field.

Abstract Theme:
I - Networks, K - Methods