SUPPLEMENTARY INFORMATION OF "AN ANOVA APPROACH FOR STATISTICAL COMPARISONS OF BRAIN NETWORKS"

daniel fraiman^{1,2} & ricardo fraiman³

CONTENTS

A1- Proof of Theorem 1	3
1.1 Notation	3
1.2 A1.1- Proof $i : \mathbb{E}(T) = 0.$	3
1.3 A1.2- Proof ii : $T \rightarrow N(0, 1)$.	4
1.4 A1.4- Proof iii: Under H_A	7
A2- Example 1	9
A3- HCP Resting-state fMRI functional networks	11
	A1- Proof of Theorem 11.1 Notation1.2 A1.1- Proof i : $\mathbb{E}(T) = 0$.1.3 A1.2- Proof ii : $T \rightarrow N(0, 1)$.1.4 A1.4- Proof iii: Under H_A A2- Example 1A3- HCP Resting-state fMRI functional networks

LIST OF FIGURES

Figure 1	Fig A1: Power of the tests as a function of the sample size for the model with parame-
-	ters $\lambda_1 = 0.5$, $\lambda_2 = 2/3$, and $\lambda_3 = 0.5$
Figure 2	Fig A2: Null hypothesis. Variance of T statistics as a function of the sample size, K for
-	the model with parameters $\lambda_1 = 0.5$, $\lambda_2 = 0.8$, and $\lambda_3 = 0.6$
Figure 3	Fig A3: Histogram of number of nodes determine by identification procedure. These
-	results correspond to the model with parameters $\lambda_1 = 0.5$, $\lambda_2 = 0.8$, $\lambda_3 = 0.6$ and K = 30. 10
Figure 4	Fig A4: Relationship between variable Right Inferiortemporal Area and variable: (A)
-	Amount of sleep, (B) Brain segmentation volume. The Spearman correlation coeffi-
	cient between both variables are shown. (C) Spearman correlation matrix between the
	highly significant variables
Figure 5	Fig A5: T–statistics as a function of (left panel) ρ and (right panel) the number of links
	for the variable <i>Picture vocabulary test</i>

LIST OF TABLES

Table 1	Variables that partitioned the subjects in groups that present very high statistical dif-
	ferences between the corresponding brain networks. Only variables with $W_3 \ge 4$ are
	included

Table 2	Behavioral variables that partitioned the subjects in groups that present high statistical
	differences between the corresponding brain networks. The W_3 , W_4 and W_5 statistics
	are presented for different networks sizes (15 / 50 / 300). Only variables with $W_3 \ge 4$
	are included

 ¹ Departamento de Matemática y Ciencias, Universidad de San Andrés, Buenos Aires, Argentina.
 ² Consejo Nacional de Investigaciones Científicas y Tecnológicas (CONICET), Buenos Aires, Argentina.
 ³ Centro de Matemática, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay.

1 A1- PROOF OF THEOREM 1

$$\mathsf{T} := \frac{\sqrt{m}}{a} \sum_{i=1}^{m} \sqrt{n_i} \left(\frac{n_i}{n_i - 1} \overline{\mathsf{d}}_{G^i}(\mathcal{M}_i) - \frac{n}{n - 1} \overline{\mathsf{d}}_{G}(\mathcal{M}_i) \right) \tag{1}$$

Theorem 1. Under the null hypothesis the statistic T verifies *i*) and *ii*), while T is sensitive to the alternative hypothesis, verifying *iii*).

- *i*) $\mathbb{E}(\mathsf{T}) = \mathsf{0}$.
- *ii)* T *is asymptotically* ($K := \min\{n_1, n_2, .., n_m\} \rightarrow \infty$) *Normal*(0,1).
- iii) Under the alternative hypothesis T will be smaller than any negative value for K large enough (The test is consistent).

1.1 Notation

Let
$$T = \frac{\sqrt{m}}{a} Z$$
 with

$$Z = \sum_{i=1}^{m} W_i$$

$$W_i = b_i D_{G^i}(\mathcal{M}_i) - c_i D_G(\mathcal{M}_i)$$

$$b_i = \frac{\sqrt{n_i}}{n_i - 1}$$

$$c_i = \frac{\sqrt{n_i}}{n - 1}$$

$$D_{G^i}(\mathcal{M}_i) = n_i \overline{d}_{G^i}(\mathcal{M}_i)$$

$$D_G(\mathcal{M}_i) = n \overline{d}_G(\mathcal{M}_i).$$

1.2 A1.1- Proof $i : \mathbb{E}(T) = 0$.

Let denote by $G_1^1, \ldots, G_{n_1}^1$ the sample networks from subpopulation 1, $G_1^2, \ldots, G_{n_2}^2$ the ones from subpopulation 2, and so on until $G_1^m, \ldots, G_{n_m}^m$ the networks from subpopulation m. Let denote without superscript G_1, \ldots, G_n the complete pooled sample of networks where $n = \sum_{i=1}^m n_i$. And let $G_1^{k\oplus}, \ldots, G_{n\oplus}^{k\oplus}$ be the pooled sample of networks without the sample k where $n_{k\oplus} = \sum_{h\neq k}^m n_h$.

The sum of the distance from the pooled sample to the average network of sample k (M_k) can be decomposed in the following way,

$$D_{G}(\mathcal{M}_{k}) = D_{G^{k}}(\mathcal{M}_{k}) + D_{G^{k\oplus}}(\mathcal{M}_{k}).$$

Where

$$\begin{split} D_{G^k}(\mathcal{M}_k) &= \mathfrak{n}_k \sum_{i < j} 2\hat{\mathfrak{p}}_k(i,j)(1 - \hat{\mathfrak{p}}_k(i,j)), \\ D_{G^{k\oplus}}(\mathcal{M}_k) &= \mathfrak{n}_{k\oplus} \big(\sum_{i < j} \hat{\mathfrak{p}}_{k\oplus}(i,j)(1 - \hat{\mathfrak{p}}_k(i,j)) + \hat{\mathfrak{p}}_k(i,j)(1 - \hat{\mathfrak{p}}_{k\oplus}(i,j)) \big), \end{split}$$

and $\hat{p}_k(i,j) = \frac{X_{i,j}^k}{n_k}$ is the proportion of times the link (i,j) appears in the sample k $(X_{ij}^k$ is the number of times link (i,j) appears in sample k), and $\hat{p}_{k\oplus}(i,j)$ the proportion of times link (i,j) appears in the sample of networks $G^{k\oplus}$.

Using the fact that under H₀ it verifies that $\mathbb{E}(\hat{p}_k(i,j)) = \mathbb{E}(\hat{p}_{k\oplus}(i,j)) =: p(i,j)$, and applying the equality $\mathbb{E}(\hat{p}(i,j)^2) = p(i,j)(1-p(i,j))/n + p(i,j)^2$ it is easy to obtain that

$$\mathbb{E}(D_{G^{k}}(\mathcal{M}_{k})) = (2n_{k} - 2)\sum_{i < j} p(i, j)(1 - p(i, j)).$$
(2)

Now, since $\hat{p}_k(i, j)$ and $\hat{p}_{k\oplus}(i, j)$ are independent we obtain,

$$\mathbb{E}\left(\mathsf{D}_{\mathsf{G}^{k\oplus}}(\mathcal{M}_k)\right) = 2\mathfrak{n}_{k\oplus}\sum_{i< j}\mathfrak{p}(i,j)(1-\mathfrak{p}(i,j)).$$

Therefore,

$$\mathbb{E}(D_{G}(\mathcal{M}_{k})) = (2n-2)\sum_{i < j} p(i,j)(1-p(i,j)),$$
(3)

and consequently

$$\mathbb{E}\left(\frac{1}{n_{k}-1}D_{G^{k}}(\mathcal{M}_{k})\right) = \mathbb{E}\left(\frac{1}{n-1}D_{G}(\mathcal{M}_{k})\right)$$

which is the same to $\mathbb{E}(W_k) = 0$, proving that $\mathbb{E}(T) = 0$

1.3 A1.2- Proof ii : $T \rightarrow N(0, 1)$.

 $\overline{d}_{G}(\mathcal{M}_{k})$ and $\overline{d}_{G^{k}}(\mathcal{M}_{k})$ verifies the central limit because they are averages of finite variance variables. Under the Null hypothesis, both random variables have expected value zero. Then W_{k} has an asymptotic Normal distribution centered in zero. Moreover, $c \sum_{k=1}^{m} W_{k}$, where c is a non-zero constant, has an asymptotic Normal distribution centered in zero which finish the proof.

Up till now, we have shown that T is asymptotically Normal centered in zero. On the following we show that the asymptotic variance is 1.

A1.3- The value a

In this proof we will use only basic properties of the variance and the moments of the Binomial distribution. The value a is a sum of many simple functions. Here we calculate each of the terms of the sum.

$$Var(T) = \frac{m}{a^2} Var(Z)$$

Since we want Var(T) = 1, $a = \sqrt{mVar(Z)}$

$$Var(Z) = \sum_{1 \leqslant k \leqslant m} Var(W_k) + 2 \sum_{1 \leqslant r < t \leqslant m} Cov(W_r, W_t)$$

$$\begin{aligned} &Var(W_k) = b_k^2 Var(D_{G^k}(\mathcal{M}_k)) + c_k^2 Var(D_G(\mathcal{M}_k)) - 2b_k c_k Cov(D_{G^k}(\mathcal{M}_k), D_G(\mathcal{M}_k)) \\ &Cov(W_r, W_t) = Cov(b_r D_{G^r}(\mathcal{M}_r), b_t D_{G^t}(\mathcal{M}_t)) - Cov(b_r D_{G^r}(\mathcal{M}_r), c_t D_G(\mathcal{M}_t)) \\ &+ Cov(c_r D_G(\mathcal{M}_r), c_t D_G(\mathcal{M}_t)) - Cov(c_r D_G(\mathcal{M}_r), b_t D_{G^t}(\mathcal{M}_t)) \end{aligned}$$

As we have shown

$$D_{G^{k}}(\mathcal{M}_{k}) = n_{k} \sum_{i < j} 2\hat{p}_{k}(i, j)(1 - \hat{p}_{k}(i, j)) = \frac{2}{n_{k}} \sum_{i < j} X_{i, j}^{k}(n_{k} - X_{i, j}^{k}),$$

and under H_0 is verified that $X_{1,1}^k, X_{1,2}^k, \dots, X_{1,s}^k, X_{2,1}^k, X_{2,2}^k, \dots, X_{s-1,s}^k$ are i.i.d. random variables with $X_{i,j}^k \sim Bin(n_k, p_{i,j})$ where s is the number of nodes in the network. And

$$D_{G}(\mathcal{M}_{k}) = D_{G^{k}}(\mathcal{M}_{k}) + D_{G^{k\oplus}}(\mathcal{M}_{k}) =$$
$$= \frac{2}{n_{k}} \sum_{i < j} X_{i,j}^{k}(n_{k} - X_{i,j}^{k}) + \frac{1}{n_{k}} \sum_{i < j} \left(n_{k\oplus}X_{i,j}^{k} + n_{k}X_{i,j}^{k\oplus} - 2X_{i,j}^{k\oplus}X_{i,j}^{k}\right)$$

with $X_{1,1}^{k\oplus}$... $_{s-1,s}^{k\oplus}$ are iid r.v. with $X_{i,j}^{k\oplus} \sim Bin(n_{k\oplus}, p_{i,j})$ and are independent of $X_{i,j}^k$ for all i, j. Now we calculate each of the above terms.

 $Var(D_{G^k}(\mathfrak{M}_k))$

$$\operatorname{Var}(D_{G^{k}}(\mathcal{M}_{k})) = (\frac{2}{n_{k}})^{2} \sum_{i < j} \operatorname{Var}(X_{i,j}^{k}(n_{k} - X_{i,j}^{k})).$$

$$\operatorname{Var}(X_{i,j}^{k}(n_{k}-X_{i,j}^{k})) = M_{2}(X_{i,j}^{k})n_{k}^{2} - 2n_{k}M_{3}(X_{i,j}^{k}) + M_{4}(X_{i,j}^{k}) - (M_{1}(X_{i,j}^{k})n_{k} - M_{2}(X_{i,j}^{k}))^{2},$$

where M_i is the i-th moment of the Binomial Distribution.

$$\operatorname{Var}(\mathsf{D}_{\mathsf{G}^{k}}(\mathfrak{M}_{k})) = (\frac{2}{\mathfrak{n}_{k}})^{2} \sum_{i < j} \mathsf{M}_{2}(\mathsf{X}_{i,j}^{k}) \mathfrak{n}_{k}^{2} - 2\mathfrak{n}_{k} \mathsf{M}_{3}(\mathsf{X}_{i,j}^{k}) + \mathsf{M}_{4}(\mathsf{X}_{i,j}^{k}) - (\mathsf{M}_{1}(\mathsf{X}_{i,j}^{k})\mathfrak{n}_{k} - \mathsf{M}_{2}(\mathsf{X}_{i,j}^{k}))^{2}.$$

 $Var(D_G(\mathcal{M}_k))$

$$Var(D_{G}(\mathcal{M}_{k})) = Var(D_{G^{k}}(\mathcal{M}_{k}) + D_{G^{k\oplus}}(\mathcal{M}_{k}))$$
$$Var(D_{G}(\mathcal{M}_{k})) = Var(D_{G^{k}}(\mathcal{M}_{k})) + Var(D_{G^{k\oplus}}(\mathcal{M}_{k})) + 2Cov(D_{G^{k}}(\mathcal{M}_{k}), D_{G^{k\oplus}}(\mathcal{M}_{k}))$$
(4)
The second term on the right

Te second term on the right,

$$\begin{aligned} \operatorname{Var}(\operatorname{D}_{G^{k\oplus}}(\mathcal{M}_{k})) &= \operatorname{Var}(\frac{1}{n_{k}}\sum_{i < j}\left(n_{k\oplus}X_{i,j}^{k} + n_{k}X_{i,j}^{k\oplus} - 2X_{i,j}^{k\oplus}X_{i,j}^{k}\right)) = \\ &= \frac{1}{n_{k}^{2}}\sum_{i < j}\operatorname{Var}\left(n_{k\oplus}X_{i,j}^{k} + n_{k}X_{i,j}^{k\oplus} - 2X_{i,j}^{k\oplus}X_{i,j}^{k}\right) \\ &= \frac{1}{n_{k}^{2}}\sum_{i < j}n_{k\oplus}^{2}\operatorname{Var}(X_{i,j}^{k}) + n_{k}^{2}\operatorname{Var}(X_{i,j}^{k\oplus}) + 4\operatorname{Var}(X_{i,j}^{k\oplus}X_{i,j}^{k}) - 4n_{k\oplus}\operatorname{Cov}(X_{i,j}^{k}, X_{i,j}^{k\oplus}X_{i,j}^{k}) + \\ &- 4n_{k}\operatorname{Cov}(X_{i,j}^{k\oplus}, X_{i,j}^{k\oplus}X_{i,j}^{k}).\end{aligned}$$

Each term can be expressed in a simply way in term of the moments of the binomial distribution. For example,

$$Cov(X_{i,j}^{k}, X_{i,j}^{k\oplus}X_{i,j}^{k}) = M_1(X_{i,j}^{k\oplus})(M_2(X_{i,j}^{k}) - M_1(X_{i,j}^{k})^2)$$

The third term on the right on eq. 4,

$$\operatorname{Cov}(\operatorname{D}_{G^{k}}(\mathcal{M}_{k}), \operatorname{D}_{G^{k\oplus}}(\mathcal{M}_{k})) = \operatorname{Cov}(\frac{2}{n_{k}}\sum_{i < j} X_{i,j}^{k}(n_{k} - X_{i,j}^{k}), \frac{1}{n_{k}}\sum_{i < j} (n_{k\oplus}X_{i,j}^{k} + n_{k}X_{i,j}^{k\oplus} - 2X_{i,j}^{k\oplus}X_{i,j}^{k})),$$

applying the independence between both random variable can be expressed as,

$$\operatorname{Cov}(\operatorname{D}_{G^{k}}(\mathcal{M}_{k}), \operatorname{D}_{G^{k\oplus}}(\mathcal{M}_{k})) = \frac{2}{n_{k}^{2}} \sum_{i < j} \left(\operatorname{Cov}(X_{i,j}^{k}n_{k}, n_{k\oplus}X_{i,j}^{k}) - 2\operatorname{Cov}(X_{i,j}^{k}n_{k}, X_{i,j}^{k\oplus}X_{i,j}^{k}) + \right)$$

$$-\operatorname{Cov}((X_{i,j}^{k})^{2},\mathfrak{n}_{k\oplus}X_{i,j}^{k})+2\operatorname{Cov}((X_{i,j}^{k})^{2},X_{i,j}^{k}X_{i,j}^{k\oplus}))$$

And again each term can be easily expressed in terms of the moments of the binomial distribution.

$$\operatorname{Cov}(\operatorname{D}_{\operatorname{G}^k}(\mathcal{M}_k),\operatorname{D}_{\operatorname{G}}(\mathcal{M}_k))$$

$$Cov(D_{G^{k}}(\mathcal{M}_{k}), D_{G}(\mathcal{M}_{k})) = Cov(D_{G^{k}}(\mathcal{M}_{k}), D_{G^{k}}(\mathcal{M}_{k}) + D_{G^{k\oplus}}(\mathcal{M}_{k}))) =$$
$$= Var(D_{G^{k}}(\mathcal{M}_{k})) + Cov(D_{G^{k}}(\mathcal{M}_{k}), D_{G^{k\oplus}}(\mathcal{M}_{k})).$$

The two terms have been previously calculated.

 $\underline{Cov}(D_{G^{r}}(\mathcal{M}_{r}), D_{G^{t}}(\mathcal{M}_{t})) \quad \text{with} \quad r \neq t$

$$\operatorname{Cov}(\operatorname{D}_{\operatorname{G}^{\operatorname{r}}}(\operatorname{\mathcal{M}}_{\operatorname{r}}),\operatorname{D}_{\operatorname{G}^{\operatorname{t}}}(\operatorname{\mathcal{M}}_{\operatorname{t}}))=0,$$

since $D_{\,G^{\,r}}(\,\mathfrak{M}_{\,r})$ and $D_{\,G^{\,t}}(\,\mathfrak{M}_{\,t}\,)$ are independent random variables

$$\underline{Cov}(D_{G^r}(\mathcal{M}_r), D_G(\mathcal{M}_t)) \text{ with } r \neq t$$

$$Cov(D_{G^{r}}(\mathcal{M}_{r}), D_{G}(\mathcal{M}_{t})) = Cov(D_{G^{r}}(\mathcal{M}_{r}), D_{G^{r}}(\mathcal{M}_{t}) + D_{G^{r\oplus}}(\mathcal{M}_{t})) =$$

= Cov(D_{G^{r}}(\mathcal{M}_{r}), D_{G^{r}}(\mathcal{M}_{t})) + Cov(D_{G^{r}}(\mathcal{M}_{r}), D_{G^{r\oplus}}(\mathcal{M}_{t}))

Now using that
$$D_{G^r}(\mathcal{M}_t) = \frac{1}{n_t} \sum_{i < j} (n_r X_{i,j}^t + n_t X_{i,j}^r - 2X_{i,j}^r X_{i,j}^t)$$
 we obtain
 $Cov(D_{G^r}(\mathcal{M}_r), D_{G^r}(\mathcal{M}_t)) = \frac{2}{n_r n_t} \sum_{i < j} Cov(n_r X_{i,j}^r, n_t X_{i,j}^r) - 2Cov(n_r X_{i,j}^r, X_{i,j}^r X_{i,j}^t) + -Cov((X_{i,j}^r)^2, n_t X_{i,j}^r) + 2Cov((X_{i,j}^r)^2, X_{i,j}^r X_{i,j}^t)$

Since $D_{\,G^{\,r}}(\mathcal{M}_{r})$ and $D_{\,G^{\,r\oplus}}(\mathcal{M}_{t})$ are independent

$$\operatorname{Cov}(\operatorname{D}_{\operatorname{G}^r}(\operatorname{\mathfrak{M}}_r),\operatorname{D}_{\operatorname{G}^r\oplus}(\operatorname{\mathfrak{M}}_t))=0$$

$$\frac{Cov(D_G(\mathcal{M}_r), D_G(\mathcal{M}_t))}{D_G(\mathcal{M}_r) = \sum_{i < j} (n - X_{i,j}^r - X_{i,j}^t - X_{i,j}^{rt\oplus}) \frac{X_{i,j}^r}{n_r} + (X_{i,j}^r + X_{i,j}^t + X_{i,j}^{rt\oplus})(1 - \frac{X_{i,j}^r}{n_r}) \text{ and } D_G(\mathcal{M}_t) = \sum_{i < j} (n - X_{i,j}^r - X_{i,j}^t - X_{i,j}^{rt\oplus}) \frac{X_{i,j}^t}{n_t} + (X_{i,j}^r + X_{i,j}^{t\oplus})(1 - \frac{X_{i,j}^r}{n_t})$$

$$\begin{split} \operatorname{Cov}(\operatorname{D}_{G}(\operatorname{M}_{r}),\operatorname{D}_{G}(\operatorname{M}_{t})) &= \sum_{i < j} \operatorname{Cov}((\operatorname{n} - \operatorname{X}_{i,j}^{r} - \operatorname{X}_{i,j}^{t} - \operatorname{X}_{i,j}^{rt\oplus}) \frac{\operatorname{X}_{i,j}^{r}}{\operatorname{n}_{r}}, (\operatorname{n} - \operatorname{X}_{i,j}^{r} - \operatorname{X}_{i,j}^{t} - \operatorname{X}_{i,j}^{rt\oplus}) \frac{\operatorname{X}_{i,j}^{t}}{\operatorname{n}_{t}}) + \\ &+ \operatorname{Cov}((\operatorname{n} - \operatorname{X}_{i,j}^{r} - \operatorname{X}_{i,j}^{t} - \operatorname{X}_{i,j}^{rt\oplus}) \frac{\operatorname{X}_{i,j}^{r}}{\operatorname{n}_{r}}, (\operatorname{X}_{i,j}^{r} + \operatorname{X}_{i,j}^{t} + \operatorname{X}_{i,j}^{rt\oplus})(1 - \frac{\operatorname{X}_{i,j}^{t}}{\operatorname{n}_{t}})) + \\ &+ \operatorname{Cov}((\operatorname{X}_{i,j}^{r} + \operatorname{X}_{i,j}^{t} + \operatorname{X}_{i,j}^{rt\oplus}))(1 - \frac{\operatorname{X}_{i,j}^{r}}{\operatorname{n}_{r}}), (\operatorname{n} - \operatorname{X}_{i,j}^{r} - \operatorname{X}_{i,j}^{t} - \operatorname{X}_{i,j}^{rt\oplus}) \frac{\operatorname{X}_{i,j}^{t}}{\operatorname{n}_{t}}) + \\ &+ \operatorname{Cov}((\operatorname{X}_{i,j}^{r} + \operatorname{X}_{i,j}^{t} + \operatorname{X}_{i,j}^{rt\oplus}))(1 - \frac{\operatorname{X}_{i,j}^{r}}{\operatorname{n}_{r}}), (\operatorname{X}_{i,j}^{r} + \operatorname{X}_{i,j}^{t} + \operatorname{X}_{i,j}^{rt\oplus}))(1 - \frac{\operatorname{X}_{i,j}^{t}}{\operatorname{n}_{t}})) \end{split}$$

From here is straighfoward to finish the expression in terms of the moments of the binomial distribution.

$$\underline{\operatorname{Cov}(\operatorname{D}_{G}(\mathcal{M}_{r}),\operatorname{D}_{G^{t}}(\mathcal{M}_{t}))}$$

.

$$\mathrm{Cov}(\mathrm{D}_{\mathrm{G}}(\mathcal{M}_{\mathrm{r}}),\mathrm{D}_{\mathrm{G}^{\mathrm{t}}}(\mathcal{M}_{\mathrm{t}}))=\mathrm{Cov}(\mathrm{D}_{\mathrm{G}^{\mathrm{t}}}(\mathcal{M}_{\mathrm{t}}),\mathrm{D}_{\mathrm{G}}(\mathcal{M}_{\mathrm{r}}))$$

The right term was already calculated.

1.4 A1.4- Proof iii: Under H_A

Let write the sample size of each subpopulation as $n_k = c_k n$ where $0 < c_k < 1$, and $\sum_{k=1}^{m} c_k = 1$. The proof is based on the fact that if H_0 *is not true* then for any d < 0 there exist a n such that

$$\mathbb{E}(\mathsf{T}) < \mathsf{d}$$

Or equivalently,

$$\lim_{n\to\infty} \mathbb{E}\left(\mathsf{T}\right) = -\infty$$

$$\mathbb{E}(\mathsf{T}) = \sum_{k=1}^{m} \frac{\sqrt{m}}{a} \sum_{k=1}^{m} \sqrt{n_k} \left(\frac{1}{n_k - 1} \mathbb{E}(\mathsf{D}_{\mathsf{G}^k}(\mathcal{M}_k)) - \frac{1}{n - 1} \mathbb{E}(\mathsf{D}_{\mathsf{G}}(\mathcal{M}_k)) \right)$$
(5)

It easy to verify that

$$\mathbb{E}(\mathsf{T}) = \frac{\sqrt{\mathfrak{m}}}{\mathfrak{a}} \sum_{i < j} \mathbb{E}\left(\mathsf{T}^{i,j}\right) := \sum_{i < j} \frac{\sqrt{\mathfrak{m}}}{\mathfrak{a}} \sum_{k=1}^{\mathfrak{m}} \sqrt{\mathfrak{n}_{k}} \left(\frac{1}{\mathfrak{n}_{k} - 1} \mathbb{E}\left(\mathsf{D}_{\mathsf{G}^{k}}^{i,j}(\mathfrak{M}_{k})\right) - \frac{1}{\mathfrak{n} - 1} \mathbb{E}\left(\mathsf{D}_{\mathsf{G}}^{i,j}(\mathfrak{M}_{k})\right)\right), \quad (6)$$

where the sum $\sum_{i < j}$ is over all links, $D_{G^k}^{i,j}(\mathcal{M}_k) = \frac{2}{n_k} X_{i,j}^k(n_k - X_{i,j}^k)$ and $D_{G^k}^{i,j}(\mathcal{M}_k) = \frac{2}{n_k} X_{i,j}^k(n_k - X_{i,j}^k) + \frac{1}{n_k} \left(n_k \oplus X_{i,j}^k + n_k \left(\sum_{h \neq k} X_{i,j}^h \right) - 2 \left(\sum_{h \neq k} X_{i,j}^h \right) X_{i,j}^k \right)$

For simplicity reasons let suppose that the first m-1 groups have a mean network \tilde{M} with elements $\tilde{M}(i,j) = p(i,j)$ and the last group m has another mean network \tilde{M}_m with elements

$$\tilde{\mathfrak{M}}_{\mathfrak{m}}(\mathfrak{i},\mathfrak{j}) = \begin{cases} & \mathfrak{p}(\mathfrak{i},\mathfrak{j}) \text{ for all } (\mathfrak{i},\mathfrak{j}) \neq (\mathfrak{i}^*,\mathfrak{j}^*) \\ & \mathfrak{q}(\mathfrak{i},\mathfrak{j}) \text{ for all } (\mathfrak{i},\mathfrak{j}) = (\mathfrak{i}^*,\mathfrak{j}^*), \end{cases}$$

with $q(i^*, j^*) \neq p(i^*, j^*)$. i.e. the mean network differ in only one link. Under this hypothesis,

$$\mathbb{E}\left(\mathsf{T}\right)=\mathbb{E}\left(\mathsf{T}^{\mathsf{i}^{*},\mathsf{j}^{*}}\right),$$

since the $\mathbb{E}(T^{i,j}) = 0$ for all $(i,j) \neq (i^*,j^*)$. Now, if we replace $D_{G^k}^{i,j}(\mathcal{M}_k)$ and $D_{G^k}^{i,j}(\mathcal{M}_k)$ and we take expectation it is easy to verify that $\mathbb{E}(T)$ is a quadric expression in $p(i^*,j^*)$ and $q(i^*,j^*)$. If we call $x = p(i^*,j^*)$ and $y = q(i^*,j^*)$, then $\mathbb{E}(T)$ verifies

$$\mathbb{E}(T) = a_1 x^2 + a_2 y^2 + a_3 x y + a_4 x + a_5 y + a_6.$$

Now we now that if x = y (null hypothesis) then $\mathbb{E}(T) = 0$. This means that the there is 1 dimensional subspace that is solution of the equation $\mathbb{E}(T) = 0$. Now, there are two possibilities for a quadric equation to verifies this last. If there exist another 1 dimensional space for the equation $\mathbb{E}(T) = 0$ then the function $\mathbb{E}(T)$ is an hyperbolic paraboloid, if not the function $\mathbb{E}(T)$ is a parabolic cylinder. In order to distinguish between these two cases we will move a little ($\varepsilon \ll 1$) to both sides of the found solution for $\mathbb{E}(T) = 0$ (the line x=y) and see if the sign of $\mathbb{E}(T)$ change. If the sign changes then $\mathbb{E}(T)$ is an hyperbolic paraboloid, if not $\mathbb{E}(T)$ is a parabolic cylinder.

We will study $\mathbb{E}(T)$ for $(x_1, y_1) = (1/2, 1/2 + \varepsilon)$ and for $(x_2, y_2) = (1/2, 1/2 - \varepsilon)$ with $\varepsilon > 0$. For simplicity we will study $\lim_{n \to \infty} \frac{1}{\sqrt{n}} \mathbb{E}(T)$ which is enough for proof ¹.

It is straightforward to see that for both (x_1, y_1) and (x_2, y_2)

$$\lim_{n\to\infty}\frac{1}{\sqrt{n}}\mathbb{E}(T) = -2(1-c_m)\sqrt{c_m}\epsilon^2,$$

¹ Based on T it is easy to see that the rate of convergence $\frac{1}{\sqrt{n}}$

which is negative value since $0 < c_m < 1$, confirming that $\mathbb{E}(T)$ is a parabolic cylinder that goes than, i.e. if $q(i^*, j^*) \neq p(i^*, j^*)$ then

$$\lim_{n\to\infty}\mathbb{E}\left(T\right)=-\infty.$$

To finish the proof we say that any other alternative hypothesis can be proved from this particular alternative scenario. For example, if there exist another (i^{**}, j^{**}) with $p(i^{**}, j^{**}) \neq q(i^{**}, j^{**})$ then

$$\mathbb{E}\left(T\right) = \mathbb{E}\left(T^{\mathfrak{i}^{*}, \mathfrak{j}^{*}}\right) + \mathbb{E}\left(T^{\mathfrak{i}^{**}, \mathfrak{j}^{**}}\right)$$

and we apply the same proof for each term. Another alternative hypothesis might be that there exist a unique (i^*, j^*) where $p_r(i^*, j^*) \neq p_s(i^*, j^*)$ for $r \neq s$ being $p_r(i^*, j^*)$ the probability of observing link (i^*, j^*) in subpopulation r. In this case $\mathbb{E}(T)$ is a quadric expression in $p_1(i^*, j^*)$, $p_2(i^*, j^*)$, ..., and $p_m(i^*, j^*)$. And the same argument can be used obtaining the same result, under the alternative hypothesis $\lim_{n \to \infty} \mathbb{E}(T) = -\infty$.

2 A2- EXAMPLE 1



Figure S1: Fig A1: Power of the tests as a function of the sample size for the model with parameters $\lambda_1 = 0.5$, $\lambda_2 = 2/3$, and $\lambda_3 = 0.5$.



Figure S2: Fig A2: **Null hypothesis.** Variance of T statistics as a function of the sample size, K for the model with parameters $\lambda_1 = 0.5$, $\lambda_2 = 0.8$, and $\lambda_3 = 0.6$.



Figure S3: Fig A3: Histogram of number of nodes determine by identification procedure. These results correspond to the model with parameters $\lambda_1 = 0.5$, $\lambda_2 = 0.8$, $\lambda_3 = 0.6$ and K = 30.

3 A3- HCP RESTING-STATE FMRI FUNCTIONAL NETWORKS

For each variable, we calculated W_3 as well as W_4 and W_5 , which counts the number of T statistics lower than -4 and -5, respectively. Using a resampled bootstrap, we obtained empirical probabilities $P(W_5 \ge 1) = 0$ (less than 1/10000) and $P(W_4 = 1) = 1/10000$. Variables with W_3 values greater than 3 are shown in Table S1 and S2.

Brain volumetric variable	W ₃	W_4	W_5
FS–R–Inferiortemporal–Area	5	5	3
FS–SupraTentorial–Vol	5	5	3
FS-R-WM-Vol	5	4	3
FS-R-Cort-GM-Vol	6	3	3
FS–BrainSeg–Vol	5	3	3
FS-Tot-WM-Vol	5	3	3
FS–Mask–Vol	5	3	3
FS–L–Middletemporal–Area	9	4	2
FS–R–Cuneus–Area	5	4	2
FS–L–Lateraloccipital–Area	4	4	2
FS–R–Superiorfrontal–Area	5	3	2
FS-BrainSeg-Vol-No-Vent	5	3	2
FS–L–Supramarginal–Area	5	3	1
FS–R–Fusiform–Area	5	2	2
FS-BrainStem-Vol	5	2	1
FS–R–Precentral–Area	5	2	1
FS–L–Superiorfrontal–Area	4	3	2
FS-L-WM-Vol	4	3	2
FS–OpticChiasm–Vol	4	2	2
FS–R–Rostralmiddlefrontal–Area	4	2	1

Table S1: Variables that partitioned the subjects in groups that present very high statistical differences between the corresponding brain networks. Only variables with $W_3 \ge 4$ are included.

Behavioral variables (label)	W ₃	W_4	W_5
Amount of sleep (PSQI_AmtSleep)	9/8/7	6/6/7	4/6/6
Cognitive flexibility (CardSort_AgeAdj)	4/3/4	3/3/4	0/3/3
Cognitive flexibility (CardSort_Unadj)	4/3/3	0/2/2	0/2/2
Motor (Strength_AgeAdj)	4/3/3	4/3/3	3/2/2
Motor (Strength_Unadj)	4/3/4	4/2/3	2/2/2
Working memory (WM_Task_2bk_Acc)	3/5/1	0/2/1	0/0/1
Relational processing (Relational_Task_Acc)	3/4/7	0/3/6	0/0/5
Delay discounting (DDisc_SV_10yr_40K)	1/5/7	0/1/6	0/0/6
Delay discounting (DDisc_AUC_4oK)	0/4/4	0/3/4	0/3/4

Table S2: Behavioral variables that partitioned the subjects in groups that present high statistical differences between the corresponding brain networks. The W_3 , W_4 and W_5 statistics are presented for different networks sizes (15 / 50 / 300). Only variables with $W_3 \ge 4$ are included.



Figure S4: Fig A4: Relationship between variable Right Inferiortemporal Area and variable: (A) Amount of sleep , (B) Brain segmentation volume. The Spearman correlation coefficient between both variables are shown. (C) Spearman correlation matrix between the highly significant variables.



Figure S5: Fig A5: T–statistics as a function of (left panel) ρ and (right panel) the number of links for the variable *Picture vocabulary test*.