

## **Large scale brain organization of anti-correlated networks and their variations in the aging brain**

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### **Introduction**

Anatomically connected networks introduce statistical dependencies in the dynamics of the connected regions, inducing functional connectivity (FC). However, FC might also occur between regions with no direct anatomical connections, due to multiple effects such as common inputs, physiological components, or the indirect effects, correlations coming from third common-neighbour regions (Friston, 2011). Functionally connected networks can be decomposing in positively and negatively correlated networks, widely known as anti-correlated networks (ACNs). In relation to ACNs, it has been shown that some pre-processing steps might enhance the presence of ACNs (Murphy et al., 2018). Other studies have also shown that ACNs might have a biological role, beyond details on the pre-processing steps (Fox et al., 2009). It has been shown the anti-correlating role of the DMN (Uddin et al., 2009; Chen et al., 2017) for some specific resting state networks (RSNs), but there is not yet a systematic work analysing large-scale organization of ACNs, which is the main purpose of this study. Moreover, we also show how the structure and organization of ACN is affected in the aging brain.

### **Methods**

Data were selected from the 1000 functional connectomes project. We chose  $N=198$  subjects from the Beijing Zang dataset (Chao-Gan, 2017), that after a quality-check selection process resulted in 192 subjects (74 male, 118 female). For the analysis in aging, we chose the “Max Planck Institut Leipzig Mind-Brain-Body Dataset – LEMON” (Babayán et al., 2019). In particular, we chose  $N_{\text{young}}=20$  (range

20-25years; 10 male, 10 female), and  $N_{old}=20$  (range 70-80 years; 10 male, 10 female). The functional images were pre-processed using the Functional Connectivity (CONN v18b) toolbox (Whitfield-Gabrieli & Nieto-Castanon, 2012). We have analysed the following 8 different RSNs: Default Mode Network (DMN), Frontoparietal Network (FPN), Sensorimotor Network (SMN), Dorsal Attention Network (DAN), Visual Network (VN), Language Network (LN), Salience Network (SN) and Cerebellar Network (CN). For the Beijing Zang dataset voxel wise multiple correction was performed using *p-FDR-corrected*  $< 10^{-14}$  and *peak to voxel p-FWE corrected*  $< 10^{-14}$ . For the Lemon dataset the correction thresholds were *p-FDR-corrected*  $< 0.05$  and *cluster size p-FDR-corrected*  $< 0.05$ .

## **Results**

Among all the 8 different RSNs analysed, the precuneus plays the major anti-correlating role, participating in 4 of the 8 ACNs. Other secondary structures playing anti-correlating roles are the superior frontal gyrus, and the posterior cingulate gyrus. When looking to differences in ACNs between young and old adults, DAN and CN are the RSNs with higher significant group differences.

## **Conclusions**

We have assessed in a systematic manner the organization and anatomy of 8 relevant ACNs in the human brain. Furthermore, we have shown how by looking only to the structure of ACNs, it is possible differentiate relevant aspects between young and old adults. Our results give special relevance to ACNs, and suggest its use for disentangle common patterns of alterations across conditions, for instance, as it occurs in several neurodegenerative diseases at early onset, or across some psychiatric conditions.

## **Keywords**

Anti-Correlated Networks,

Default Mode Network

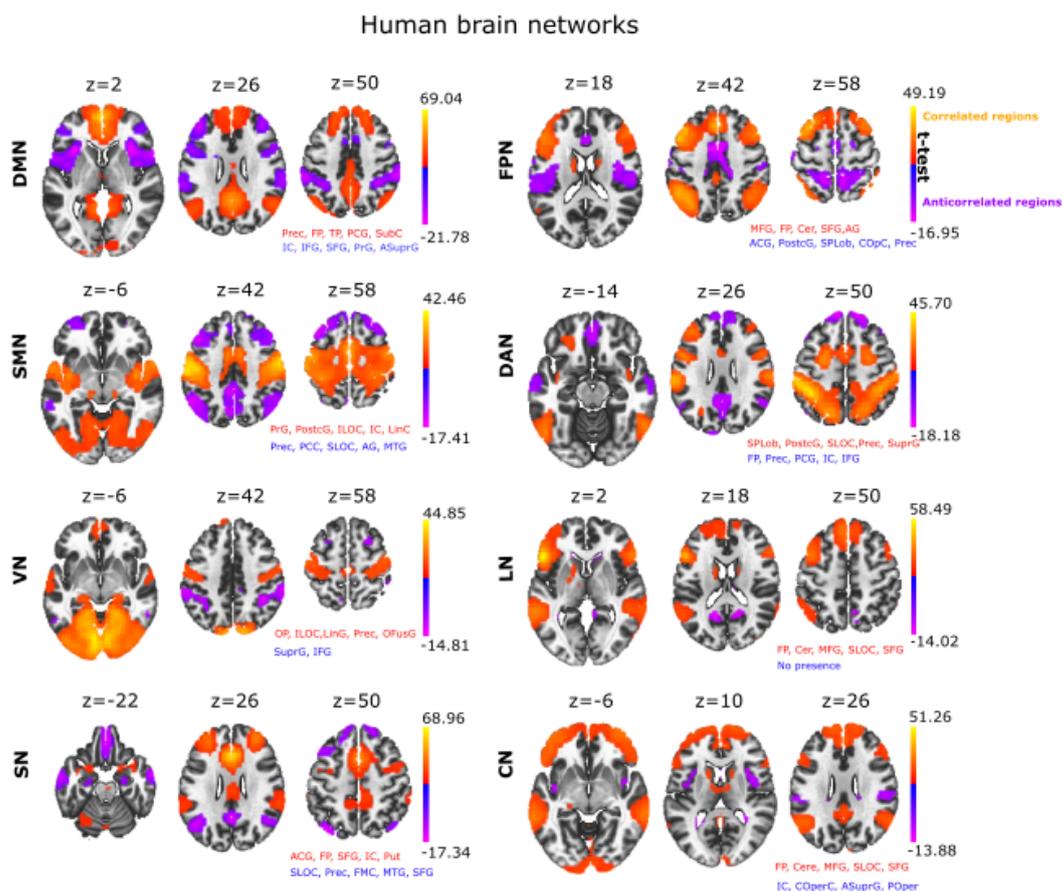
Precuneus

Aging

Functional MRI

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Anticorrelated networks old vs young adults

