Supplementary Materials for

Key environmental effects on the developing functional connectome: a 3T resting-state fMRI study on young twins.

Emma Tassi^, Eleonora Maggioni^, Maddalena Mauri, Corrado Fagnani, Nivedita Agarwal, Anna Maria Bianchi, Maria A. Stazi, Maria Nobile, Paolo Brambilla*

^ Equally contributing authors.

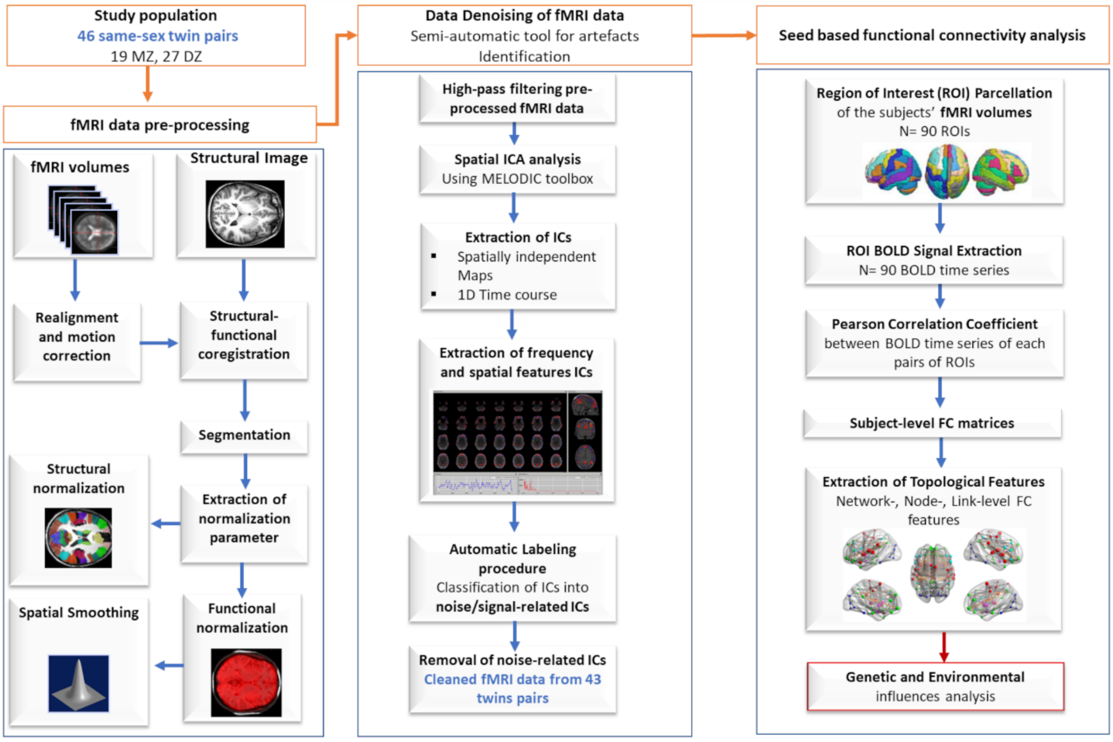
* Paolo Brambilla
Department of Neurosciences and Mental Health, Fondazione IRCCS Ca'Granda Ospedale Maggiore Policlinico, Milan, Italy.
Tel. +39 02-55032717.
Email: paolo.brambilla1@unimi.it

The document includes:

Supplementary **Figures S1 and S2**.

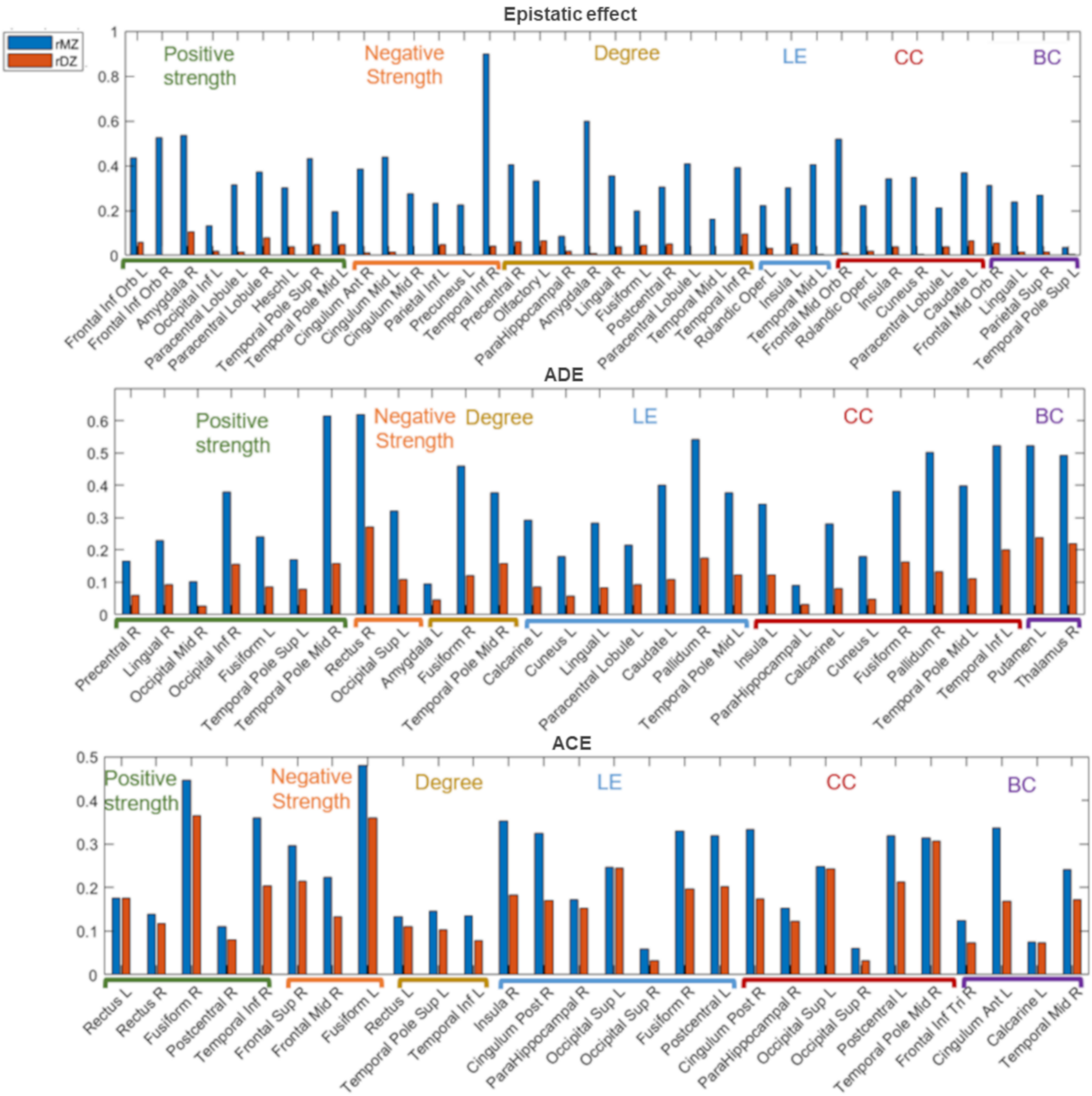
Supplementary **Tables S1, S2 and S3**.

Fig. S1. Schematic illustration of fMRI processing steps.



The resting-state fMRI raw data from 46 same-sex twin pairs were pre-processed using SPM12. As follow, the data denoising of the pre-processed fMRI data was applied by the use of a semiautomatic tool for artefacts identification and subsequently the artefactual independent components (ICs) were regressed out from the data. At this step, the subjects associated with a percentage of noise-related ICs > 75% and their siblings were excluded from the analyses, resulting in a dataset composed of 43 twin pairs. Seed-based functional connectivity (FC) analyses were applied to the subject's fMRI volumes to extract the subject-level FC matrices based on the Automated Anatomic Atlas (AAL) parcellation. FC matrices were extracted by computing the Pearson correlation coefficients between BOLD time series. Multiple brain network features at different spatial scales (brain-, node- and link-level) were extracted from each subject's FC matrix and entered in the statistical analyses.

Fig. S2. Barplots of r_{MZ} and r_{DZ} values for node-level FC metrics.



$\boldsymbol{r_{MZ}}$ and $\boldsymbol{r_{DZ}}$ values associated with node-level FC metrics under epistasis (first panel), ADE effects (second panel), and ACE effects (third panel). $\boldsymbol{r_{MZ}}$ values are illustrated in blue, while $\boldsymbol{r_{DZ}}$ values are reported in red. $\boldsymbol{r_{DZ}}$: intra-pair phenotypic correlation in DZ pairs. $\boldsymbol{r_{MZ}}$: intra-pair phenotypic correlation in MZ pairs. Along the x-axis of each panel are reported the ROIs related to node-level FC metrics influenced by epistatic effect (first panel), ADE effects (second panel) and ACE effects (third panel). All the node-level metrics meeting the criteria for epistatic, ADE, or ACE effects are illustrated.

Table S1. Description of node-level functional connectivity (FC) metrics extracted for the analysis.

Node-level FC metrics	**Description**
Local efficiency	It describes the regional efficiency indicating the integration of each node. It represents the global efficiency computed on the neighbourhood of the node (extracted from binarized FC matrix).
Clustering coefficient	It describes the ability for functional segregation and efficiency of local information transfer (extracted from binarized FC matrix).
Degree	It represents number of links connected to the node indicating how many connections a node has to other nodes (extracted from binarized FC matrix).
Strength of weights	It indicates the average weight of connections each node has with other nodes. Calculated as the sum of the nodes associated to positive and negative weights (extracted from weighted FC matrix). The *strength of positive weight* is calculated as the sum of the links connected to the nodes associated to a positive correlation with the others and represents the total positive strength of the node, and how much this node communicates in synchrony with the others. The *strength of negative weight* is calculated as the sum of the links connected to the nodes associated to a negative correlation with the others and represents the total negative strength of the node, and how much this node communicates in asynchrony with the others.
Betweenees centrality	It indicates the fraction of all shortest paths in the network that contain a given node, if a node has a highest fraction of shortest paths, more communication across the network will pass through this node (extracted from binarized FC matrix).

Table S2. Description of Global-level functional connectivity (FC) metrics extracted for the analysis.

Global FC metrics	**Description**
Global efficiency	It is estimated as the average inverse shortest path length in the network, representing the integration over the whole brain network (extracted from binarized FC matrix).
Characteristic path length	It is calculated as the average shortest path length in the network and representing how "efficiently" the brain is connected (extracted from binarized FC matrix).
Degree	It represents the average degree in the network (see Table S1, extracted from binarized FC matrix).
Density	It indicates the fraction of present connections out of all possible connections, indicate how densely connected is a graph (extracted from binarized FC matrix).
Louvain modularity	It represents the modularity of a network and quantifies the "strength" of partition of a network into modules (also called communities and clusters). Louvain method is an efficient method to identify communities in large network. The method is a greedy optimization that attempts to optimize the modularity of a partition of a network by: firstly, it looks for small communities optimizing modularity locally, then it aggregates nodes belonging to the same community and builds a new network whose nodes are the communities (extracted from binarized FC matrix).

Table S3. Automated Anatomical Labeling (AAL) atlas regions included in the resting state networks (RSNs).

RSN	**AAL regions**
Salience Network	Superior frontal gyrus, dorsolateral Middle frontal gyrus Insula Amygdala Temporal pole: superior temporal gyrus Anterior cingulate and paracingulate gyri Superior frontal gyrus, medial
Default Mode Network	Anterior cingulate and paracingulate gyri Superior frontal gyrus, medial Median cingulate and paracingulate gyri Posterior cingulate gyrus Hippocampus Parahippocampal gyrus Middle occipital gyrus Temporal pole: middle temporal gyrus Superior frontal gyrus, orbital part Middle frontal gyrus, orbital part Inferior frontal gyrus, orbital part Superior frontal gyrus, medial part Angular gyrus Precuneus Inferior frontal gyrus, opercular part Inferior frontal gyrus, triangular part
Central Executive Network	Superior frontal gyrus, orbital part Middle frontal gyrus, orbital part Inferior frontal gyrus, orbital part Superior frontal gyrus, medial part Angular gyrus Precuneus Inferior frontal gyrus, opercular part Inferior frontal gyrus, triangular part Superior parietal gyrus Inferior parietal, supramarginal and angular gyri Supramarginal gyrus Caudate nucleus Middle temporal gyrus Inferior temporal gyrus
Motor Network	Precentral gyrus Postcentral gyrus Supplementary motor area Paracentral lobule
Visual Network	Cuneus Lingual gyrus Calcarine fissure and surrounding cortex Superior occipital gyrus Middle occipital gyrus Inferior occipital gyrus Fusiform gyrus
Auditory Network	Heschl gyrus Superior temporal gyrus Rolandic operculum Thalamus
Basal Ganglia Network	Thalamus Lenticular nucleus, putamen Lenticular nucleus, pallidum

RSN, Resting-state network.