Graduate School of
Systemic Neurosciences
LMU Munich

Regression of functional brain networks in early Alzheimer‘s disease

Valentin Riedl[1,3,4], Christian Sorg[2], Afra Wohlschläger[3]
[1]Dept. of Neurology, [2]Dept. of Psychiatry, [3]Dept. of Neuroradiology, Univ.Hospital Rechts der Isar, Technische Universität (TUM), Munich
[4]Graduate School of Systemic Neurosciences, Munich Center for Neurosciences, Ludwig-Maximilians-Universität (LMU), Munich

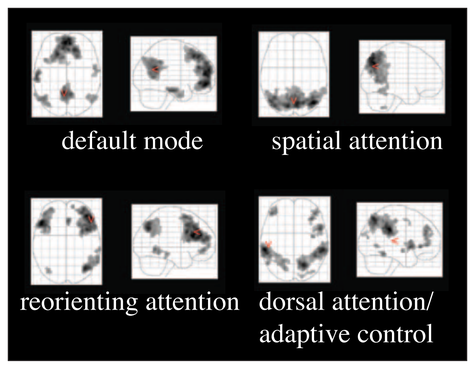
The maturing brain has recently been analyzed with resting-state functional connectivity MRI (rs-fcMRI). Spatial patterns of synchronous, intrinsic brain activity were found to be similar to resting-state networks (RSNs) previously described in adults. However distant regions of the default network have only been sparsely connected. The brain functional connectivity (FC) has also been analyzed in subjects at a later stage of life span. Here a disruption of long-range connections was reported that split the default network in an anterior and posterior part.

Recently we described selectively disturbed default and executive attention networks among several RSNs in patients with mild cognitive impairment (MCI) at high risk for Alzheimer‘s Disease (AD). Are long-range connections in age-associated disorders like AD affected by pathological changes prior to short-range connections?

We analyzed RSNs of healthy subjects and patients with MCI at high risk for AD for the influence of regional proximity on FC.

„It is necessary to study not only parts and processes in isolation, but also to solve the decisive problems found in organization and order unifying them, resulting from dynamic interaction of parts, and making the behavior of the parts different when studied in isolation or within the whole. ...“

Ludwig von Bertalanffy, General System Theory

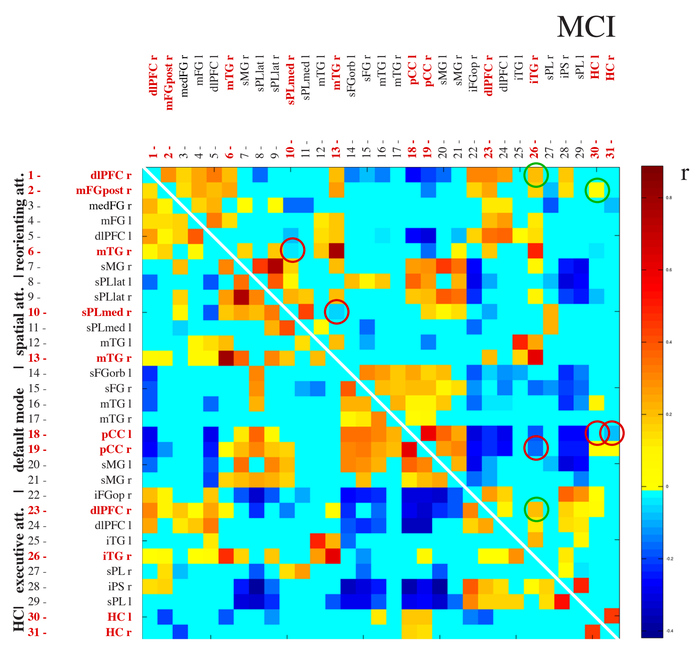


Results
MCI compared to Healthy Controls

- no correlation in 4 right hemispheric pairs and left pCC/HC (red circles)

- increased correlation in right dlPFC/ iTG and right mFGpost/HC left (green circles)

° = p < 0.05 (FDR corrected)



Methods
Functional Connectivity

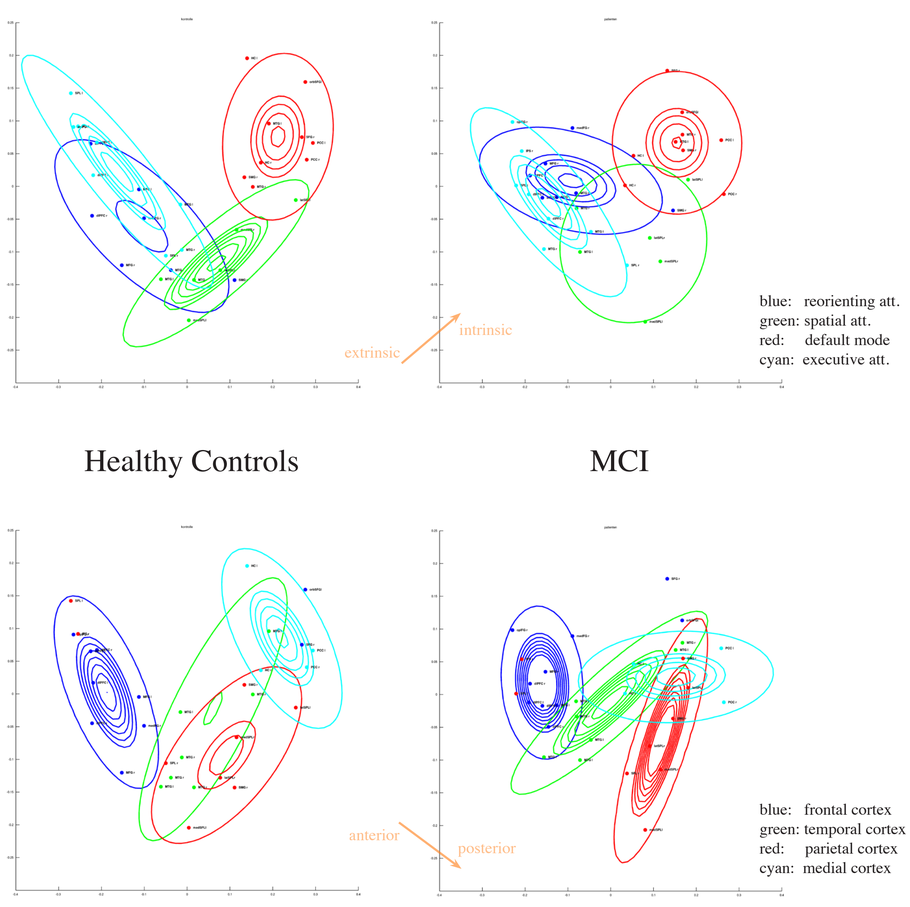
We constructed spherical ROIs (r=6mm) around previously described peak voxel of 4 RSNs and extracted the voxelwise BOLD timecourse (tc). For each ROI the first eigenvector was derived with singular value decomposition yielding the most prominent proportion in the BOLD signal. The tc was bandpass-filtered (0.009<f<0.079Hz) and the signal from global gray matter, CSF and deep white matter was removed from the data through linear regression. A Fisher’s Z-transformation was applied to yield normal distribution. We then calculated the pairwise **Pearson‘s correlation coefficients** (r) for the **31 ROIs** in both groups. Between-Group effects were calculated using two-sample t-tests and a correction for multiple comparisons was applied.

Results
2-D functional distance space

The cross-correlation matrices of Healthy Controls (left) and MCI (right) transformed in a 2-D functional distance space.

Regions with strong positive correlation are plotted close to each other while anti-correlated regions are far apart.

For visualization purposes clusters have been identified with contour plots based on a Gaussian Mixture distribution.



Methods
Transformation in a Functional Distance Space

The cross-correlation matrices of both groups were transformed in a two/three-dimensional functional space using **multi-dimensional scaling (MDS)**. The purpose of MDS is to provide a visual representation of the pattern of proximities (i.e., similarities or distances) among a set of objects (e.g. distances of several cities are projected on a map). To best conform the maps of all subjects a final **procrustes analysis** was applied. Procrustes method is used to align several shapes by rotating, shifting and stretching similar to warping images in the SPM normalization step.

We provide evidence for a disruption of interlobar long-range connections in early stages of AD. The transformation of the correlation matrix in a functional distance space further suggests an arrangement of the brain space along two axes: a structural (anterior-posterior) and a functional (intrinsic-extrinsic) axis. In the light of findings in developmental rs-fcMRI we interpret these results as a regression of functional brain networks in early AD that have been developed during lifetime while short-range connections are highly preserved.

Georges Buffon (1755): Taxonomy of dog species