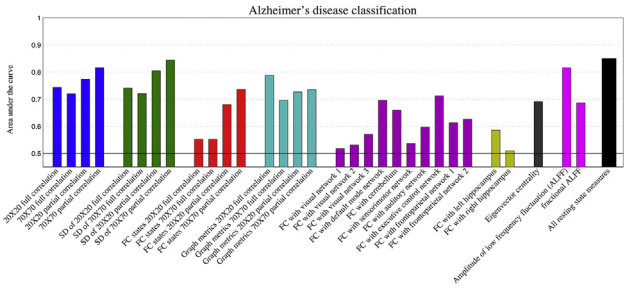
Model tested	F-value for model	P-value for model	β-coefficients	P-value for predictor
Cohort 1	3.17	0.0196*		
Age	–	–	0.000	0.46
Sex	–	–	0.004	0.17
Education	–	–	-0.001	0.06
Animal Fluency	–	–	0.001	0.00*
Cohort 2	4.70	0.0035		–
Age	–	–	-0.001	0.07
Sex	–	–	0.009	0.07
Education	–	–	-0.000	0.84
Animal Fluency	–	–	0.001	0.00*
Cohort 1	3.73	.0087		-
Age	–	–	0.000	0.89
Sex	–	–	0.004	0.20
Education	–	–	-0.001	0.27
Composite Language Fluency Score	–	–	0.004	0.00*
Cohort 2	4.50	.0044		–
Age	–	–	-0.001	0.01
Sex	–	–	0.008	0.12
Education	–	–	0.000	0.97
Composite Language Fluency Score	–	–	0.003	0.01*

decline (SCD, 22), mild cognitive impairment (MCI, 12), and AD (11). Cohort2 was a replicate sample of 58 older adult participants from the Indiana Memory and Aging study (CN, 13; SCD, 16; MCI, 21; AD, 8). Subjects underwent baseline rsfMRI; image data were processed with an in-house pipeline according to Power et al. [1]. Functional connectivity (FC) matrices were generated, which included FC data from 278 functionally-derived gray matter regions [2]. A data-driven connectivity approach (connICA) [3] was employed to extract independent FC patterns and how much each FC-pattern was present in each subject (weights). FC pattern weights were used as the dependent variable in a multilinear regression model with cognitive variables as predictors (Cognitive Complaint [4] and Cognitive Change [5] Index scores, episodic memory, executive function, animal fluency, and composite language fluency scores), with inclusion of nuisance variables. **Results:** Both datasets revealed a prominent resting state network pattern, as reported in Contreras et al [6]. In both cohorts, the RSN pattern was positively associated with animal and composite language fluency scores. Both language fluency measures were predictive of RSN pattern ($p<.005$, Table 1) demonstrating that participants with lower language fluency scores had lower FC within the canonical RSN pattern. **Conclusions:** Deficient performance on language fluency tests may be a good predictor of aberrant brain connectivity in early stages of AD. [1] Power et al(2014)Neuroimage; [2]Shen et al(2011)NeuroImage [3]Amico et al(2016)NeuroImage [4] Saykin et al(2006)Neurology [5] Rattanabannakit et al(2016)J Alzheimer's Dis [6] Contreras et al(2017)Alzheimers&Dementia.

IC-P-028 A COMPREHENSIVE ANALYSIS OF RESTING STATE FMRI MEASURES TO CLASSIFY INDIVIDUAL PATIENTS WITH ALZHEIMER'S DISEASE

Frank de Vos[1,2,3], Marisa Koini[4], Tijn M. Schouten[1,2,3], Stephan Seiler[4], Jeroen van der Grond[2], Anita Lechner[4], Reinhold Schmidt[4], Mark de Rooij[1], Serge A. R. B. Rombouts[1,2,3], *[1]Leiden University, Leiden, Netherlands;*



[2]Leiden University Medical Center, Leiden, Netherlands; [3]Leiden Institute for Brain and Cognition, Leiden, Netherlands; [4]Medical University of Graz, Graz, Austria. Contact e-mail: f.de.vos@fsw.leidenuniv.nl

Background: Alzheimer's disease (AD) patients show altered patterns of functional connectivity (FC) on resting state functional magnetic resonance imaging (RSfMRI) scans. It is yet unclear which RSfMRI measures are most informative for the individual classification of AD patients. **Methods:** We investigated this using RSfMRI scans from 77 AD patients (MMSE $= 20.4 \pm 4.5$) and 173 controls (MMSE $= 27.5 \pm 1.8$). We calculated i) FC matrices between resting state components as obtained with independent component analysis (ICA), ii) the dynamics of these FC matrices using a sliding window approach, iii) we distinguished five FC states and administered how long each subject resided in each of these five states, and iv) we calculated the graph properties (e.g., connection degree, and clustering coefficient) of the FC matrices. Furthermore, for each voxel we calculated v) FC with 10 resting state networks using dual regression, vi) FC with the hippocampus, vii) eigenvector centrality, and viii) the amplitude of low frequency fluctuations (ALFF). These eight measures were used separately as predictors in an elastic net logistic regression, and combined in a group lasso logistic regression model. We calculated the area under the receiver operating characteristic curve plots (AUC) to determine classification performance. **Results:** The AUC values ranged between 0.51 and 0.84 and the highest were found for the FC matrices (0.82), FC dynamics (0.84) and ALFF (0.82). The combination of all measures resulted in an AUC of 0.85. **Conclusions:** We show that it is possible to obtain moderate to good AD classification using RSfMRI scans. FC matrices, FC dynamics and ALFF are most discriminative and the combination of all the resting state measures improves classification accuracy slightly.

IC-P-029 GAUSSIAN MARKOV RANDOM FIELDS FOR ASSESSING INTERMODAL REGIONAL ASSOCIATIONS IN PRODROMAL ALZHEIMER'S DISEASE

Martin Dyrba[1], Michel J. Grothe[1], Harald Binder[2], Thomas Kirste[3], Stefan J. Teipel[1,4], *[1]German Center for Neurodegenerative Diseases (DZNE), Rostock, Germany; [2]Institute of Medical Biostatistics, Epidemiology and Informatics, University Medical Center, Mainz, Germany; [3]University of Rostock, Rostock, Germany; [4]Department of Psychosomatic Medicine, University Medicine Rostock, Rostock, Germany. Contact e-mail: martin.dyrba@dzne.de*

Background: Alzheimer's disease (AD) is characterized by a cascade of pathological processes that can be assessed in vivo using different neuroimaging methods. Recent research suggests a systematic sequence of pathogenic events on a global biomarker level, but little is known about the associations and

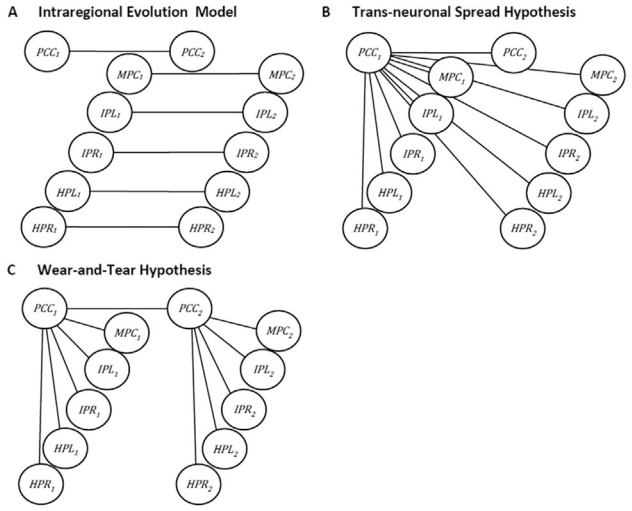


Figure 1. Representative graph structures for different hypotheses regarding the spread of Alzheimer's disease. The first imaging modality is located on the left side of each subfigure, the second modality is located on the right side. Both modalities are connected depending on the specific hypothesis. Abbreviations: HPL, HPR – left and right hippocampus, IPL, IPR – left and right inferior parietal cortex, MPC – medial prefrontal cortex, PCC – posterior cingulate cortex.

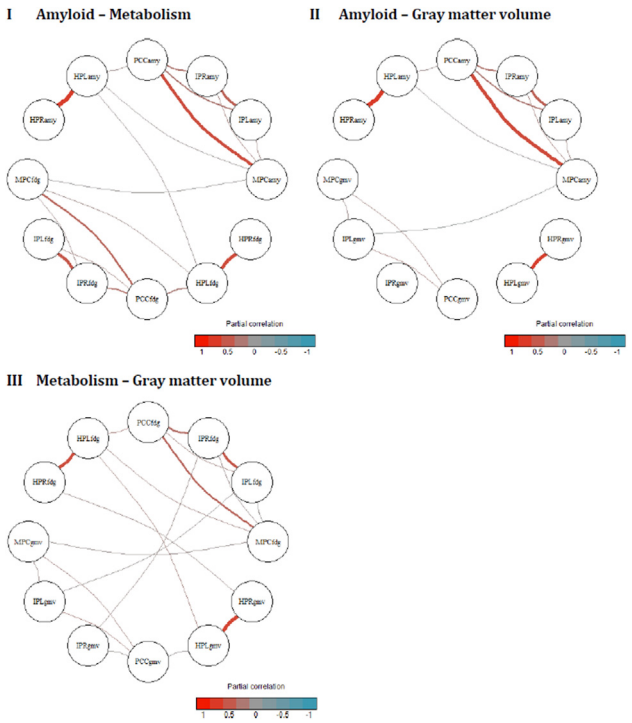


Figure 2. Graph structures and partial correlation between nodes obtained from Gaussian Markov random fields. Edges represent the mean partial correlation across the 10000 cross-validation iterations, thresholded at a significance level of $P < 0.05$.
Abbreviations: amy – amyloid-β, fdg – fluorodeoxyglucose metabolism, gmv – gray matter volume, HPL, HPR – left and right hippocampus, IPL, IPR - left and right inferior parietal cortex, MPC – medial prefrontal cortex, PCC – posterior cingulate cortex.

Table 1
Jaccard similarity coefficient for the graph structures learned from the data and the manually specified models

Modalities	Model A	Model B	Model C	Hub node
Amyloid –	0,08±0,02	0,14±0,00	0,26±0,01	HPL
Metabolism	–	0,10±0,00	0,22±0,01	IPL
	–	0,18±0,01	**0,42±0,02 ***	MPC
	–	0,14±0,00	0,36±0,02 *	PCC
Amyloid –	0.02±0.02	0.14±0.02	0.28±0.04	HPL
Gray matter	–	0.12±0.01	0.27±0.04	IPL
volume	–	0.17±0.01	0.30±0.03	MPC
	–	0.17±0.01	**0.40±0.03 ***	PCC
Metabolism –	0.23±0.02	0.13±0.01	0.23±0.02	HPL
Gray matter	–	0.13±0.01	0.25±0.03	IPL
volume	–	0.21±0.01	0.30±0.02	MPC
	–	0.17±0.03	**0.35±0.03 ***	PCC

Mean and standard deviation of the Jaccard similarity coefficient for comparing the set of edges obtained from Gaussian graphical models and the manually specified models for the different hypotheses regarding the spread of Alzheimer's disease. Asterisk indicates significant difference of the Jaccard index for the best models in comparison to all other models within the respective pair of modalities ($P < 0.05$).
Abbreviations: Models A, B, and C refer to the networks given in Figure 1. HPL – left hippocampus, IPL – left inferior parietal cortex, MPC – medial prefrontal cortex, PCC – posterior cingulate cortex.

dependencies of distinct lesion patterns on a regional level. Markov random fields are a probabilistic graphical modeling approach that represent the interaction between individual random variables by an undirected graph. We propose the novel application of this approach to study the inter-regional associations and dependencies between multimodal imaging markers of AD pathology, and to compare different hypotheses regarding the spread of the disease. **Methods:** We retrieved multimodal imaging data from 398 subjects with mild cognitive impairment enrolled in the Alzheimer's Disease Neuroimaging Initiative (ADNI). Mean amyloid load (AV45-PET), glucose metabolism (FDG-PET), and gray matter volume (MRI) were calculated for the six principle nodes of the default mode network – a functional network of brain regions that appears to be preferentially targeted by AD. Gaussian Markov random fields were fitted to the data and estimated the partial correlation between each pair of regions and imaging modalities. The resulting models were compared to previously defined graph structures representing three different hypotheses regarding the spread of the disease: the "intraregional evolution model", the "trans-neuronal spread" hypothesis, and the "wear-and-tear" hypothesis, (Figure 1 A–C). Evaluation was conducted using tenfold cross-validation with 1000 repetitions. **Results:** For all pairs of modalities, the estimated graph structures (Figure 2) were most similar to the "wear-and-tear" hypothesis of disease vulnerability (Table 1). For the pairs amyloid-β/gray matter volume and metabolism/gray matter volume, the posterior cingulate cortex provided the main hub node with strongest edges to various other regions. For the pair amyloid-β/metabolism, the hub node medial prefrontal cortex provided best fit. Although strongest associations were found within each modality, significant associations between modalities were most matching the intraregional evolution model (Figure 2). **Conclusions:** Gaussian Markov random field models offer a convenient framework for studying the associations of distinct lesion patterns in AD. They afford great potential to complement traditional multiple regression analyses in multimodal neuroimaging research.