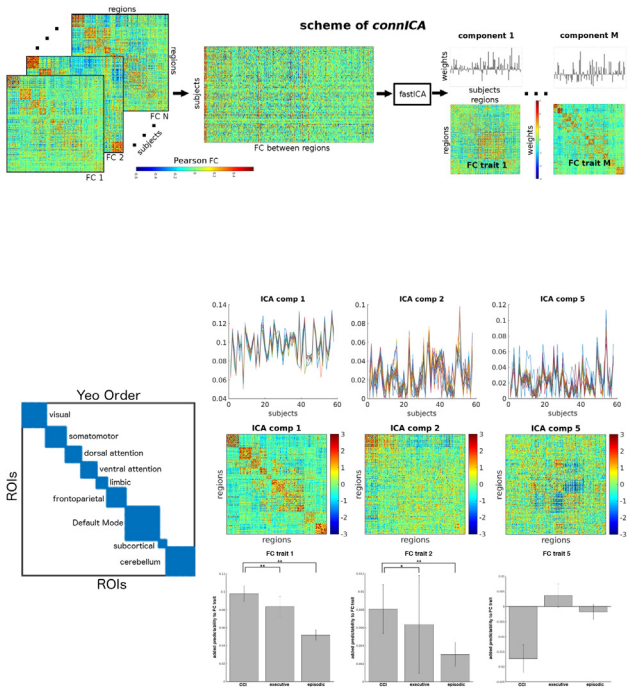

can be grouped into resting-state networks (RSNs) allowing analysis of higher-order changes within and between networks. Here we investigate the relationship of self-perceived cognitive changes to rsfMRI FC changes in a sample from the Indiana Memory and Aging Study. **Methods:** Participants included 58 older adults classified as cognitively normal (CN, 13), subjective cognitive decline (SCD, 16), early amnestic MCI (EMCI, 5), late MCI (LMCI, 16), and mild AD dementia (AD, 8) who underwent baseline rsfMRI processed with an in-house pipeline after Power et al, [1] to extract FC matrices based on a functional parcellation including 278 regions. An independent component analysis (ICA) connectivity data-driven approach (*connICA*) was used to extract FC independent patterns (FC traits). FastICA decomposition (15 independent components) was performed over a matrix of all subjects FC connectivity profiles (Figure 1). Each component signal was then used as a response in a multilinear regression model with cognitive variables (Cognitive Complaint Index (CCI) [2] scores, episodic memory and executive function domain scores) serving as the predictors and nuisance variables (age, gender, and education) included as covariates. **Results:** Two *connICA* components were strongly associated with CCI scores (FC-traits 1, 2). FC trait 1 involves a decrease in FC within each RSN whereas FC trait 2 involves an increased FC within specific somatomotor regions, and increased inter-RSN FC between somatomotor and dorsal attention networks and a general FC decrease between somatomotor and other RSNs. In both cases CCI is shown to be the best predictor of FC traits 1 and 2. FC trait 5 could not be attributed to a specific variable but is worth noting due to its robust finding (Figure 2). **Conclusions:** Self-reported cognitive complaints are strongly associated with a pattern of specific rsFC network changes as the disease progresses. Further examination of psychometric performance and FC patterns is required.

[1] Power et al (2014) Neuroimage; [2] Saykin et al. (2006) Neurology.

IC-03-04 NETWORK-BASED TAU DEPOSITION PATTERNS ARE RELATED TO FUNCTIONAL NETWORK FAILURE LARGELY VIA BETA-AMYLOID ACROSS THE ALZHEIMER'S SPECTRUM

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Background: The cascading network failure model of Alzheimer's disease (AD) pathophysiology hypothesizes that synaptic activity related to shifts in large-scale functional network organization is causally related to observed beta-amyloid accumulation via alteration in amyloid precursor protein processing. Once the large-scale network reorganization interacts with vulnerable brain systems, a tau-related neurodegenerative process initiates within that system. To test these predications we investigated the relationship between Tau-PET, task-free fMRI, and beta amyloid-PET in a cross-sectional sample spanning the Alzheimer's disease spectrum. **Methods:** Tau-PET (AV-1451), beta amyloid-PET (PiB), and TF-fMRI were obtained in a cohort of subjects across the AD spectrum ($n = 218$). All subjects who were clinically impaired (MCI = 12, dementia = 29) had PiB SUVR > 1.5. Tau-PET scans were intensity normalized to the cerebellar gray matter, spatially normalized to standard space, and smoothed. An independent component analysis was performed, with biologically relevant components being identified via a strong amyloid effect (Bonferroni corrected $p < 0.01$). A goodness-of-fit (GOF) analysis of these components with a functional connectivity atlas was then performed. Tau-PET memory system component scores were included in a mediation analyses with PiB-PET and a marker of functional network failure we term the network failure quotient (NFQ). **Results:** Five biologically relevant tau-PET components were identified. These components had high GOF scores with visual, executive, and memory-related networks likely reflecting phenotypic heterogeneity in the AD cohort given the visual and executive components were associated with age-of-

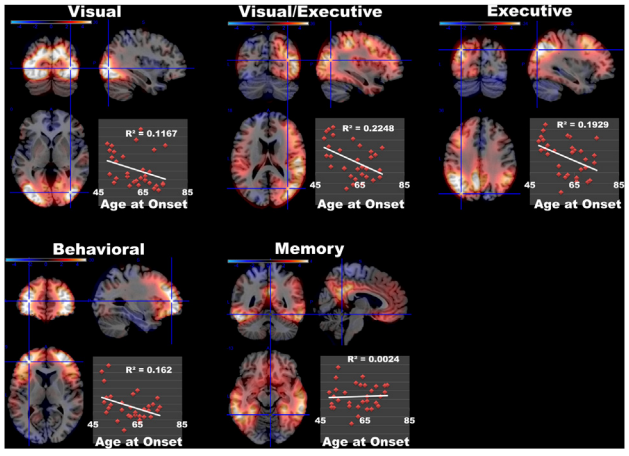

Figure. The spatial extent of the five biologically relevant Tau-PET independent components are overlaid on orthogonal slices of a template brain (color bar encodes z-score from -5 to 5). The cognitive associations of the functional connectivity atlas components associated with each Tau-PET pattern are listed above. Inset, the component scores are plotted vs. age-of-onset for the dementia cases. Note that the memory Tau-PET component is elevated across age-of-onset.

onset, but the memory component was elevated in cases independent of age-of -onset (Figure). The memory-related Tau-PET component was associated with PiB-PET (beta=0.59, p<0.001) and NFQ (beta = 0.30, p<0.001). A mediation analysis showed a strong mediation effect by PiB-PET (mediation effect [95% CI] = 0.85 [0.23, 1.41], p<0.001) on the relationship between NFQ and tau-PET (direct effect [95% CI] = 0.30 [-0.01, 0.57], p = 0.08). **Conclusions:** Tau deposits in visual, executive, and memory-related networks which may reflect phenotypic heterogeneity in AD. Consistent with the CNF model of AD, direct examination of tau-PET and functional connectivity in the same subjects demonstrates a strong association of network failure with tau that is largely mediated by beta-amyloid.

IC-03-05 EEG DIRECTED CONNECTIVITY FROM POSTERIOR BRAIN REGIONS IS DECREASED IN DEMENTIA WITH LEWY BODIES: A COMPARISON WITH ALZHEIMER'S DISEASE AND CONTROLS

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Background: Attentional deficits in dementia with Lewy bodies (DLB) could be caused by disruption in directed information flow between the frontal and parietal brain regions involved in attention networks. Therefore, directed connectivity between brain regions might be disrupted in DLB and relate to the clinical syndrome of DLB. To investigate this hypothesis, we analyzed the EEG directed connectivity pattern in DLB and compared that with controls, and patients with Alzheimer's disease (AD). Furthermore, we tested whether potential disturbance in directed connectivity in DLB was correlated with attentional deficits. **Methods:** Resting-state EEG recordings were obtained in DLB and AD patients, and controls (N=66 per group, matched for age and gender). Phase transfer entropy (PTE), a novel phase-based measure for directed connectivity, was used to measure directed connectivity in the groups for the theta, alpha and beta frequency band. TMT test part B (TMT-B) was included as a measure of attention in DLB. **Results:** A posterior-to-anterior PTE gradient, with occipital channels driving the frontal channels, was found in controls in all frequency bands. This posterior-to-anterior gradient was largely lost in DLB in the alpha band (p<.05). In the beta band, posterior brain regions were less driving in information flow in AD patients than in DLB patients and controls. A higher mean PTE gradient in the posterior brain regions in the beta band correlated with better performance on the TMT-B test in DLB patients (N=36, rho=-.37; p=.03). **Conclusions:** The common posterior-to-anterior pattern of directed connectivity in controls is disturbed in DLB patients mainly in the alpha band, and in AD patients mainly in the beta band. Disrupted alpha band directed connectivity may underlie the pathophysiology of DLB and differentiate between DLB and AD. Impaired directed connectivity between frontal and parietal brain areas in the beta band might be the underlying pathophysiological mechanism of attentional deficits in DLB. Future studies with neuroimaging tools with higher temporal and spatial resolution such as magnetoencephalography are needed to explore the specific pathophysiological role of directed connectivity in the beta band, and in various anatomical regions in DLB.

SATURDAY, JULY 23, 2016
ALZHEIMER'S IMAGING CONSORTIUM (AIC)
ICI-01
WHAT HAVE WE LEARNED?

ICI-01-01 WHAT HAVE WE LEARNED?

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Abstract not available.

SATURDAY, JULY 23, 2016
ALZHEIMER'S IMAGING CONSORTIUM (AIC)
ICI-02
ALZHEIMER'S DISEASE IMAGING BIOMARKERS AND AGING

ICI-02-01 ALZHEIMER'S DISEASE IMAGING BIOMARKERS AND AGING

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Abstract not available.

SATURDAY, JULY 23, 2016
ALZHEIMER'S IMAGING CONSORTIUM (AIC)
ICI-03
CONTROVERSY DEBATE: ALZHEIMER'S DISEASE — SINGLE VERSUS MULTIPLE BRAIN NETWORK DISORDER

ICI-03-01 CONTROVERSY DEBATE: SINGLE BRAIN NETWORK DISORDER

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Background: In Alzheimer's disease, both rise and propagation of neurodegenerative changes are linked with macroscopic brain networks. The default mode network, which comprises midline structures of temporal, parietal, and prefrontal lobes, is of special interest, as suggested as the primary target of AD. **Methods:** Review of previous findings from human multi-modal imaging and animal research. **Results:** Brain changes of several dimensions and modalities, partly interrelated, affect primarly the default mode network. **Conclusions:** The talk presents and discusses main findings and problems for the view that AD is a default mode network disorder.

ICI-03-02 CONTROVERSY DEBATE: MULTIPLE BRAIN NETWORK DISORDER

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Abstract not available.