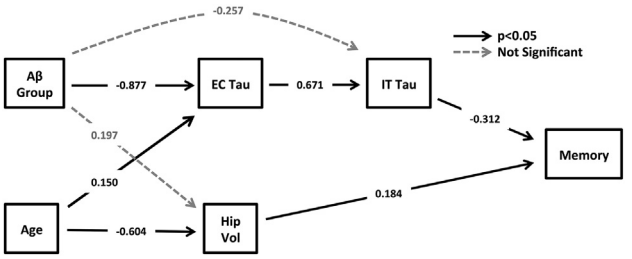

1B-C). Although Tau was related to hippocampal volume among Aβ+ (EC: r= -0.28, IT: r= -0.29), the strength of these relationships were smaller than the association between age and hippocampal volume in Aβ+ (r= -0.52). Among Aβ-, 5.3% of the total variance in memory was explained by age, EC Tau, IT Tau, and hippocampal volume, with age accounting for the most unique variance (ΔR^2= 1.7%). Among Aβ+, 32.5% of the total variance in memory was explained by age, EC Tau, IT Tau, and hippocampal volume, with IT Tau accounting for the most unique variance (ΔR^2= 17.8%). Path analysis provided support for a model in which both EC and IT Tau are related to Aβ whereas hippocampal volume is related to age. Furthermore, EC Tau is more proximal to Aβ and IT Tau is more proximal to memory (Figure 2). **Conclusions:** These results suggest that hippocampal volume largely reflects non-Aβ age-related etiologies whereas Tau is more specific for early AD processes during the asymptomatic stage of AD. Our results are consistent with a model by which Aβ exacerbates Tau in entorhinal cortex and catalyzes the spread of Tau into adjacent neocortex, which subsequently results in subtle memory impairment.

IC-02-04 AXONAL DENSITY IS ASSOCIATED WITH SUBJECTIVE COGNITIVE DECLINE (SCD) IN OLDER ADULTS ASSESSED USING THE COGNITIVE CHANGE INDEX

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Background: Converging evidence suggests that the pathophysiologic processes in the brains of Alzheimer's disease (AD) patients begin decades before symptoms occur[1-3]. Individuals in the preclinical stages of AD often report self-perceived decline in cognitive functions. The self-perception of cognitive decline can be assessed via the cognitive change index (CCI)[4,5], a recently proposed measure of perceived neuropsychological function focusing on the memory, executive, and language domains from both self and informant perspectives. In this study, we examine the association of CCI with a novel diffusion metric for axonal density. The axonal density metric is derived via a three-compartmental model, Neurite Orientation Distribution and Density Imaging (NODDI)[6]. **Methods:** Sixty-one participants with cognitively normal (CN, N=21), subjective cognitive decline (SCD, N=23) and mild cognitive impairment (MCI, N=17) underwent Hybrid Diffusion Imaging (HYDI)[7,8] that consists of five b-value shells. Diffusion images were corrected for motion, eddy and geometric distortion[9] prior to nonlinear transformation to standard MNI space using ANTS registration[10]. Median values of diffusion metrics including DTI, NODDI, and q-space analysis were extracted from skeletonized 48 white matter (WM) ROIs provided in the JHU atlas[11]. General linear regression analyses were performed to test associations between diffusion metrics and CCI scores adjusted for age, sex, and education. For comparisons of demographic and cognitive variables, ANOVAs were employed with Tukey's tests followed by post-hoc t-tests. **Results:** The three groups did not differ significantly in age, sex, and education distribution (Table 1). Strong associations ($p<0.001$) between CCI and diffusion metrics were found in ROIs belonging to the limbic system. Specifically, fractional anisotropy (FA) of DTI in the right stria terminalis had negative correlation with CCI-12 (i.e., episodic memory) ($p<0.001$, Figure 1).

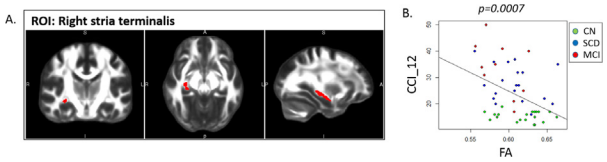

Figure 1. ROI map and scatter plot of CCI score and fractional anisotropy (FA). A. The ROI in red denotes the right stria terminalis. B. FA of diffusion tensor imaging (DTI) negatively correlated with CCI-12 (episodic memory) with p=0.0007. Age, sex and education were adjusted in the linear regression analysis. Green dots denote cognitively normal (CN); blue dots denote subjective cognitive decline (SCD); red dots denote mild cognitive impairment (MCI); and the black solid line denotes the regression line.

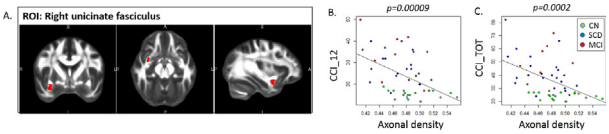

Figure 2. ROI map and scatter plot of CCI score and axonal density. A. The ROI in red denotes the right uncinate fasciculus. B. Axonal density negatively correlated with both CCI-12 (episodic memory) with p=0.00009 and CCI-TOT (20 items) with p=0.0002. Age, sex and education were adjusted in the linear regression analysis. Green dots denote cognitively normal (CN); blue dots denote subjective cognitive decline (SCD); red dots denote mild cognitive impairment (MCI); and the black solid line denotes the regression line.

Table 1
Demographic and cognitive comparisons of the three cohorts' characteristics

	CN	MCI	SCD	F/χ^2	p value	SCD-CN	MCI-CN	MCI-SCD
Age (yrs)	68.1 (5.8)	67.9 (10)	69.7 (10.3)	0.236	0.79	1	0.84	0.8
Sex (M:F)	6:15	9:14	7:10	0.384	0.68	0.76	0.71	0.99
Education (yrs)	17 (2.2)	16.5 (2.6)	16.1 (2.9)	0.505	0.61	0.82	0.58	0.9
CCI_12	15.3 (1.9)	27.6 (6.8)	33.6 (10.3)	33.471	$p<1\times10^{-5}$	$p<1\times10^{-5}$	$p<1\times10^{-5}$	p<0.05
CCI_TOT	24.3 (2.6)	41 (11)	51 (17.6)	24.682	$p<1\times10^{-5}$	$p<1\times10^{-5}$	$p<1\times10^{-5}$	p<0.05
CCI_INF12	15.6 (6)	16.1 (5.7)	32.7 (11.3)	22.029	$p<1\times10^{-5}$	0.97	$p<1\times10^{-5}$	$p<1\times10^{-5}$
CCI_INFTOT	25.7 (10.1)	25.7 (8.8)	53.3 (19.4)	21.3	$p<1\times10^{-5}$	1	$p<1\times10^{-5}$	$p<1\times10^{-5}$

Axonal density in the right uncinate fasciculus negatively correlated with both CCI-12 and CCI-TOT (20 item) ($p<0.001$, Figure 2). Other ROIs had no significant correlations. **Conclusions:** These results suggest that lower axonal density and fiber coherence are risk factors for self-perceived memory decline. The two most vulnerable white matter tracts - the right stria terminalis and uncinate fasciculus, connect between the amygdala and hippocampus - two of the areas that show the earliest disease-associated changes. References: 1. Villemagne, V.L., S. Burnham, P. Bourgeat, B. Brown, K.A. Ellis, O. Salvado, C. Szoeke, S.L. Macaulay, R. Martins, P. Maruff, D. Ames, C.C. Rowe, C.L. Masters, B. Australian Imaging, and G. Lifestyle Research, Amyloid beta deposition, neurodegeneration, and cognitive decline in sporadic Alzheimer's disease: a prospective cohort study. Lancet Neurol, 2013. 12(4): p. 357-67. 2. Jack, C.R., Jr., V.J. Lowe, S.D. Weigand, HJ. Wiste, M.L. Senjem, D.S. Knopman, M.M. Shiung, J.L. Gunter, B.F. Boeve, B.J. Kemp, M. Weiner, R.C. Petersen, and I. Alzheimer's Disease Neuroimaging, Serial PIB and MRI in normal, mild cognitive impairment and Alzheimer's disease: implications for sequence of pathological events in Alzheimer's disease. Brain, 2009. 132(Pt 5): p. 1355-65. 3. Sperling, R.A., P.S. Aisen, L.A. Beckett, D.A. Bennett, S. Craft, A.M. Fagan, T. Iwatsubo, C.R. Jack, Jr., J. Kaye, T.J. Montine, D.C. Park, E.M. Reiman, C.C. Rowe, E. Siemers, Y. Stern, K. Yaffe, M.C. Carrillo, B. Thies, M. Morrison-Bogorad, M.V. Wagster, and C.H. Phelps, Toward defining the preclinical stages of Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement, 2011. 7(3): p. 280-92. 4. Saykin, A.J., H.A. Wishart, L.A. Rabin, R.B. Santulli, L.A. Flashman, J.D. West, T.L. McHugh, and A.C. Mamourian, Older adults with cognitive complaints show brain atrophy similar to that of amnestic MCI. Neurology, 2006. 67(5): p. 834-42. 5. Rattanabannakit, C., S.L. Risacher, S. Gao, K.A. Lane, S.A. Brown, B.C. McDonald, F.W. Unverzagt, L.G. Apostolova, A.J. Saykin, and M.R. Farlow, The Cognitive Change Index as a Measure of Self and Informant Perception of Cognitive Decline: Relation to Neuropsychological Tests. J Alzheimers Dis, 2016. 51(4): p. 1145-55. 6. Zhang, H., T. Schneider, C.A. Wheeler-Kingshott, and D.C. Alexander, NODDI: practical in vivo neurite orientation dispersion and density imaging of the human brain. Neuroimage, 2012. 61(4): p. 1000-16. 7. Wu, Y.C. and A.L. Alexander, Hybrid diffusion imaging. Neuroimage, 2007. 36(3): p. 617-29. 8. Kodiweera, C., A.L. Alexander, J. Harezlak, T.W. McAllister, and Y.C. Wu, Age effects and sex differences in human brain white matter of young to middle-aged adults: A DTI, NODDI, and q-space study. Neuroimage, 2016. 128: p. 180-92. 9. Yamada, H., O. Abe, T. Shizukuishi, J. Kikuta, T. Shinozaki, K. Dezawa, A. Nagano, M. Matsuda, H. Haradome, and Y. Imamura, Efficacy of distortion correction on diffusion imaging: comparison of FSL eddy and eddy_correct using 30 and 60 directions diffusion encoding. PLoS One, 2014. 9(11): p. e112411. 10. Avants, B.B., N.J. Tustison, G. Song, P.A. Cook, A. Klein, and J.C. Gee, A reproducible evaluation of ANTs similarity metric performance in brain image registration. Neuroimage, 2011. 54(3): p. 2033-44. 11. Oishi, K., K. Zilles, K. Amunts, A. Faria, H. Jiang, X. Li, K. Akhter, K. Hua, R. Woods, A.W. Toga, G.B. Pike, P. Rosa-Neto, A. Evans, J. Zhang, H. Huang, M.I. Miller, P.C. van Zijl, J. Mazziotta, and S. Mori, Human brain white matter atlas: identification and assignment of common anatomical structures in superficial white matter. Neuroimage, 2008. 43(3): p. 447-57.

IC-02-05 ABNORMAL STRUCTURAL BRAIN CONNECTOME IN INDIVIDUALS WITH PRECLINICAL ALZHEIMER'S DISEASE

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Background: Alzheimer's disease has a long preclinical phase during which amyloid pathology and neurodegeneration accumulate in the brain without producing cognitive deficits. It is currently unclear whether these early disease stages are associated with a progressive disruption in the communication between brain regions that might lead to clinical decline and dementia. **Methods:** In this study we assessed the organization of the structural networks in cognitively normal (CN) individuals harbouring amyloid pathology (A+N-), neurodegeneration (A-N+) or both (A+N+). We combined graph theory with diffusion tensor imaging to investigate integration, segregation and centrality measures in the brain connectome of the previous groups. **Results:** At baseline, our findings revealed a disrupted network topology characterized by larger paths, lower efficiency, increased clustering and modularity in CN A-N+ and CN A+N+. After two years, CN A+N+ showed a progressive increase in the clustering, whereas no changes were observed in the other groups. Network topology correlated with cognitive speed in all groups and with memory performance specifically in CN A+N+. **Conclusions:** Altogether, our findings suggest that amyloid pathology is not sufficient to disrupt structural network topology, whereas neurodegeneration is. In contrast to CN A-N+, network organization in CN A+N+ individuals continued to decline over time and was associated with memory functions.

SATURDAY, JULY 15, 2017
ALZHEIMER'S IMAGING CONSORTIUM
IC-03
NON-ALZHEIMER'S DISEASE PATHOPHYSIOLOGY

IC-03-01 WHAT HAPPENS TO THE HIPPOCAMPUS 12 MONTHS AFTER TRAINING? LONGITUDINAL LINEAR MIXED-EFFECTS MODEL ANALYSIS OF MILD COGNITIVE IMPAIRMENT IN THE SMART TRIAL

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