(VAN), default mode network, and dorsal attention network) was assessed using template based rotation, an approach designed for use with existing network parcellations. A linear regression model with backward elimination ($p<0.1$ cut-off) was utilized with the FAQ as the dependent variable and the 4 networks as the predictors of interest. Covariates included age, sex, American National Adult Reading Test intelligence quotient (AMNART IQ, a proxy of premorbid IQ), processing speed, episodic memory, and fMRI confounders (signal-to-noise ratio, movement, and bad volumes). **Results:** There was a significant association between greater IADL impairment and reduced FPCN connectivity (β=-29.76, partial r(pr)=-0.36, p=0.03) and increased VAN connectivity (β=37.44, pr=0.40, p=0.02). Covariates retained in the model included premorbid IQ (β=0.26, pr=0.42, p=0.01), processing speed (β=-0.12, pr=-0.37, p=0.03), episodic memory (β=-0.11, pr=-0.29, p=0.09), and movement (β=27.61, pr=0.33, p=0.05). The overall model was significant (p=0.005) and accounted for 41% of the variance. There was no significant association with the other networks. **Conclusions:** These results suggest that IADL impairment in MCI relates to a complex pattern of both reduced and increased connectivity in networks spanning frontal and parietal regions. Similar findings have been reported in a study using a global functioning measure, which consists of both IADL and cognition. Furthermore, reduced FPCN connectivity has been associated with greater apathy, which has been associated with IADL impairment, and increased VAN connectivity has been associated with greater executive dysfunction, which has been associated with IADL impairment.

P3-163 INSULIN RESISTANCE AND CEREBRAL AMYLOID DEPOSITION IN COGNITIVELY HEALTHY AND PRECLINICAL AD SUBJECTS

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Background: Insulin resistance is a risk factor for Alzheimer's disease (AD) although the mechanisms linking insulin resistance with AD remain unclearly defined. **Methods:** We measured fasting metabolic biomarkers (insulin, glucose) in non-demented subjects who also had Florbetapir-PET imaging (n=50) to assess the cerebral amyloid burden. A subset of these individuals (n=27) also underwent the hyperinsulinemic-euglycemic clamp to quantify peripheral glucose disposal. We hypothesized that subjects with impaired fasting glucose (IFG; fasting glucose $\geq$100mg/dL) would exhibit greater cerebral amyloid burden compared to individuals with normoglycemia (fasting glucose $<$100mg/dL). **Results:** Subjects with IFG (n=15) exhibited greater cerebral amyloid deposition compared to those with normoglycemia (n=35) in the Posterior Cingulate Gyrus (SUVR of 1.19 (0.24) vs 1.07 (0.14), p=0.04) and a trend to greater amyloid deposition in the Precuneus (SUVR of 1.27 (0.33) vs. 1.13 (0.18), p=0.06). Cerebral amyloid burden was not significantly different across groups in the Anterior Cingulate Gyrus, Inferior Medial Frontal Gyrus, Lateral Temporal Lobe, and Superior Parietal Lobule. Interestingly, IFG was associated with isolated elevations in glucose levels while fasting insulin levels were not different than the normoglycemic group. Further, metabolic testing with the hyperinsulinemic-euglycemic clamp (n=27) demonstrated lower glucose disposal was associated with IFG compared to normoglycemia (IFG: 3.8 mg/kg$\times$min [1.1] vs 6.4 mg/kg$\times$min [2.4]). **Conclusions:** This indicates peripheral mechanisms of insulin resistance underlie dysfunctional glucoregulation in the IFG group despite similar fasting insulin levels. This data supports a potential relationship between impaired glucose metabolism and cerebral amyloid deposition in specific brain areas.

P3-164 LESS DAILY COMPUTER USE IS RELATED TO SMALLER HIPPOCAMPAL VOLUMES IN DEMENTIA-FREE ELDERLY

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Background: Unobtrusive continuous in-home monitoring may be a more sensitive means of detecting early functional changes associated with conversion to mild cognitive impairment and dementia in older individuals than traditional testing methods acquired sporadically over time. **Methods:** Twenty-nine dementia-free elderly volunteers (mean age 87.4, MMSE 28.2) enrolled in the Intelligent Systems for Assessing Aging Change study underwent 3T brain MRI. FreeSurfer was used to determine gray matter (GM) and hippocampal volumes. White matter hyperintensities (WMH) were derived using customized software. In-home computer use (CPU) was calculated using daily mouse movement detection and averaged over a one month period surrounding the time of their MRI visit. A multivariate logistic regression was performed with outcome of either high ($>$ 25 min/day) or low ($<$ 25 min/day) average computer use. A voxel based morphometry analysis was also performed to identify relationships between CPU and regional GM density. T1 images were brain extracted and then linearly aligned to the MNI-152 template and averaged to create a study specific template. All T1 images were then non-linearly aligned to this template while the degree of expansion or contraction was calculated. This transform was then applied to segmented GM tissue masks which were modulated by the Jacobian and then used for permutation testing in a model which also accounted for age and gender. **Results:** In the univariate analysis, less CPU was associated with smaller hippocampal volumes, but not with either total GM or WMH volumes. In a multivariate regression adjusted for age, gender, and intracranial volume, less CPU was associated with smaller hippocampal volume ($p = 0.027$). Voxel-wise analysis demonstrated that greater CPU was associated with increased GM density in the: right hippocampus, left hippocampus, left lingual gyrus, right inferior temporal gyrus, left superior temporal gyrus and right cingulate gyrus **Conclusions:** Daily computer use is related to brain regions linked to memory function and the

Table 1
Regions in which VBM identified significantly reduced GM density in comparison with less daily computer use.

	Coordinates				Cluster size	
Talairach Region	Side	X	Y	Z	Voxels	Volume (mm^3)
Hippocampus	Rt	-28.4	9.3	-21	1044	8352
Hippocampus	Lt	25.7	9.7	-18.7	770	6160
Lingual Gyrus	Lt	10.3	74.8	4.7	99	792
Inferior Temporal Gyrus	Rt	-63.5	28.1	-19.3	94	752
Superior Temporal Gyrus	Lt	46.9	-9.9	-20.1	81	648
Cingulate Gyrus	Rt	-1	-14	38.8	53	424
Middle Temporal Gyrus	Lt	43.1	-5.7	-35.8	25	200

processing of visual and spatial stimuli, areas previously shown to be associated with conversion to Alzheimer's dementia. Findings support the use of continuous in-home monitoring as a sensitive method to detect meaningful changes in older individuals at risk for dementia.

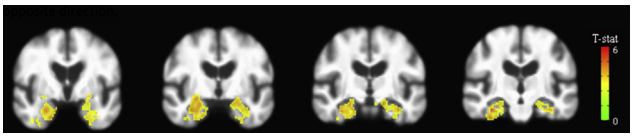

Figure 1. VBM analysis. Colored voxels indicate regions of decreased GM density significantly associated with less daily computer use ($p<0.05$).

P3-165 LOCAL AMYLOID-B TOXICITY IN LARGE INTRINSIC BRAIN NETWORKS IN COGNITIVELY HEALTHY ELDERLY

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Background: Considerable in vitro and animal data suggests that Aβ, even in the absence of tau tangles, has adverse effects on neuronal dysfunction, supporting the hypothesis that neuronal dysfunction is due in part to direct Aβ toxicity that is not completely mediated by tau. Although previous studies demonstrated the effects of global Aβ burden on the default mode network in cognitively normal elderly individuals, effects of local network Aβ burden on the other large-scale intrinsic connectivity networks (ICNs) are not yet clear in asymptomatic individuals. In this study, we aimed to investigate the effects of both global and local Aβ deposition on various cortical ICNs in older adults with normal cognition. **Methods:** Fifty-three elderly subjects with normal cognition were included. We characterized the association of Aβ burden with intrinsic connectivity changes in a wide range of functional networks, including working memory, attention, motor and perceptual timing, and visual detection networks, as well as resting-state default mode network. Aβ deposition was quantified both globally,

Table
Coefficients of determination (R^2) of the endogenous latent variables inferred by partial least squares regression analyses to assess the amount of variance in functional connectivity explained by global Aβ burden and ICN Aβ burden.

ICN	
Global Aβ burden	
ICN Aβ burden	
Default mode network (DMN)	
	0.23
	0.29
Dorsal attention network (dAN)	
	NS
	0.39
Episodic memory network (EMN)	
	NS
	0.19
Executive control network (ECN)	
	0.34
	0.46
Salience processing network (SPN)	
	NS
	0.34
Sensory motor network (SMN)	
	0.27
	0.21
Supplementary motor area network (SMA)	
	0.33
	0.49
Visual network (VN)	
	0.15
	0.11

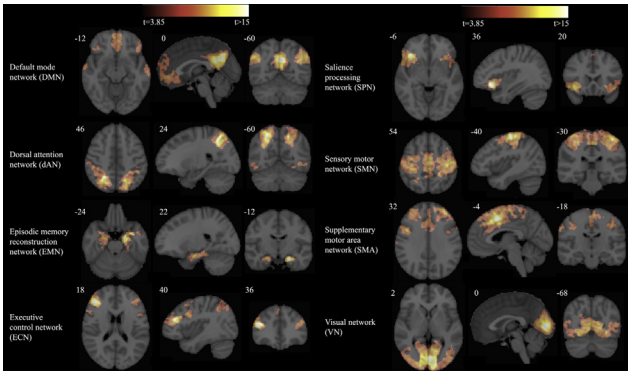

Figure 1. Spatial maps of the ICNs of interest identified by seed-to-voxel based analysis of Aβ- and ApoE ε4 non-carrier subjects.

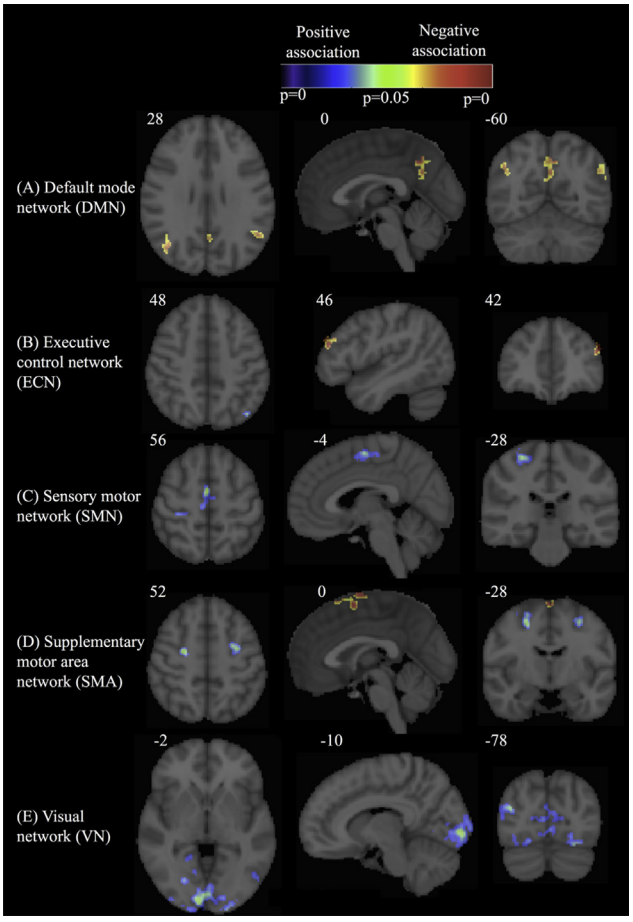

Figure 2. Voxel-based maps of latent variables inferred by partial least squares regression analyses of functional connectivity and global Aβ burden associations.