

Supplemental Figure 1. Box plots of Regional Tau-PET SUVR by Clinically Defined Groups.

Box plots of regional tau-PET SUVR (without partial volume correction [PVC]) by cognitively defined groups based on clinical diagnosis and amyloid-PET status. The area under the receiver operating characteristic curve (AUROC) is shown in the right margin for cognitively unimpaired individuals with normal amyloid versus abnormal amyloid (first column of AUROC values) and for abnormal amyloid cognitively impaired versus all cognitively unimpaired individuals (second column of AUROC values). Regions are ordered by AUROC based on cognitively impaired versus cognitively unimpaired individuals. Most individual regions provide very good discrimination between cognitively unimpaired and cognitively impaired groups. Both medial temporal and extra-temporal regions provide highest AUROC values.

Supplemental Figure 2. Association of Age and Amyloid-PET SUVR Among Cognitively Unimpaired Individuals.

Scatter plot of amyloid-PET SUVR versus age with Spearman rank correlation among cognitively unimpaired individuals.

Supplemental Figure 3. Percentage of Individuals with Elevated Tau-PET Signal in Each Region.

The plot shows the percentages of individuals with elevated tau-PET signal by region within low-normal amyloid cognitively unimpaired (light green), intermediate-normal amyloid cognitively unimpaired (dark green), high-abnormal amyloid cognitively unimpaired (blue), and high-abnormal amyloid cognitively impaired (orange) groups. After adjusting for age and correcting for multiple comparisons, two regions more frequently had elevated tau-PET

signal in the intermediate compared to the low amyloid cognitively unimpaired group (amygdala and frontal inferior orbital, indicated by asterisks) and there were no significant differences between the intermediate and high amyloid cognitively unimpaired groups. High-abnormal amyloid cognitively impaired individuals had the higher percentage of elevated tau-PET in all regions. The low amyloid group continued to have elevated tau-PET signal in regions that were widespread (frontal superior orbital, inferior occipital, frontal mid orbital, precuneus and others).

Supplemental Figure 4. Dendrogram of Hierarchical Cluster findings in Cognitively Unimpaired Participants.

The dendrogram summarizes the full hierarchical clustering among cognitively unimpaired individuals beginning with every individual in their own group and ending with all individuals in one combined group. The vertical axis represents the distance between clusters and a horizontal line drawn at any point defines the number of clusters. The blue line indicates our selection of the four clusters characterized in this study and represents a balance of choosing enough distinct clusters to possibly see interesting patterns while keeping the number of clusters tractable. The cluster numbers correspond to the order shown in Fig. 3.

Supplemental Figure 5. Dendrogram of Hierarchical Cluster findings in Cognitively Impaired Participants.

The dendrogram summarizes the full hierarchical clustering among cognitively impaired individuals beginning with every individual in their own group and ending with all individuals in one combined group. The vertical axis represents the distance between clusters and a horizontal line drawn at any point defines the number of clusters. The blue line indicates our selection of the three clusters characterized in this study and represents a

balance of choosing enough distinct clusters to possibly see interesting patterns while keeping the number of clusters tractable. The cluster numbers correspond to the order shown in Fig. 3.

Supplemental Figure 6. Box plots of Regional Tau-PET SUV_r by Hierarchical Cluster in Select Regions. Box plots of tau-PET SUV_r for regions not shown in Fig. 3 by the four clusters among cognitively unimpaired individuals and three clusters among cognitively impaired individuals. Clinical diagnosis and amyloid-PET status is represented by different colors: normal amyloid cognitively unimpaired, green; abnormal amyloid cognitively unimpaired, blue; abnormal amyloid amnestic mild cognitive impairment (aMCI), purple; abnormal amyloid dementia due to Alzheimer's disease (ADD), orange.

Supplemental Figure 7. Box plots of Regional Tau-PET SUV_r by Age, Amyloid-PET status and Diagnosis Sub-categorization. Box plots of tau-PET SUV_r for regions not shown in Fig. 4 by clinical diagnosis, amyloid-PET status, and age. Clinical diagnosis and amyloid-PET status are represented with different colors: normal amyloid cognitively unimpaired, green; abnormal amyloid cognitively unimpaired, blue; abnormal amyloid amnestic mild cognitive impairment (aMCI), purple; abnormal amyloid dementia due to Alzheimer's disease (ADD), orange. Extra medial temporal differences are seen cognitively unimpaired >50 normal amyloid group vs. the cognitively unimpaired normal amyloid <50 group (all are significant but the highest magnitude regions include, inferior temporal, inferior occipital, mid occipital, fusiform, and superior orbital frontal regions)

Supplemental Figure 8. Summation Images of Hierarchical Clusters Among cognitively unimpaired and cognitively impaired.

Tau-PET images representing the summed data from all participants in the respective clusters are shown. Globally increasing tau-PET signal is seen in cognitively unimpaired clusters as: 1 < 2 < 3 < 4. The temporal regions show subtly elevated tau-PET signal in cognitively unimpaired clusters 3 and 4 as compared to the other cognitively unimpaired clusters (red arrows). Higher frontal, posterior cingulate and temporal region tau-PET signal is seen in cognitively impaired clusters 2 and 3 (yellow arrows) as compared to cognitively impaired cluster 1 with the highest in cluster 3. The cognitively impaired cluster 1 has greater temporal and posterior cingulate tau-PET signal than cognitively unimpaired cluster 4 (yellow arrows). All images were color normalized and the color scale showing SUVr values is shown.