interaction; F=5.38, p=0.03). APOE-ε4 carriers had lower NAA/mI compared to non-carriers (t=2.24, p=0.03). tCho/Cr in white matter was associated with Aß (r= -0.53 p=0.004) and WMH (r= -0.51; p=0.006); APOE-ε4 carriers with high WMH showed strongest reductions of tCho/Cr (significant APOE-ε4 x WMH interaction, F=6.45, p=0.02). **Conclusions:** These findings suggest that a neurometabolic signature of AD, defined by metabolic correlates of Aß and APOE-ε4 in older adults, consists of reduced NAA/mI in gray matter and reduced tCho/Cr in white matter. We speculate that these metabolic differences reflect neuronal impairment, glial activation, and altered choline metabolism. This neurometabolic signature of AD is also associated with WMH, both independently and synergistically with Aß and APOE-ε4, emphasizing the importance of small-vessel cerebrovascular disease for AD pathogenesis.

IC-P-019 EFFECTS OF USING A NOVEL LONGITUDINAL PROCESSING PIPELINE FOR MEASURING CHANGE OVER TIME IN PIB-PET

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Background: Accurate and reliable automated measures of change-over-time in amyloid PET are crucial to observational and clinical trials for Alzheimer's disease. Previous works have examined how varying methodological choices, such as reference region, affect change measurements computed from cross-sectional (computed intra-timepoint) measurements. This work examines the effects of using longitudinal (simultaneous cross-timepoint) measurement methods. **Methods:** We implemented a novel, automated longitudinal pipeline. Corresponding serial T1-weighted images were coregistered using a group-wise ANTs nonlinear registration to produce a mean-space T1-weighted single-subject template image (T1-SST). This T1-SST was segmented with SPM12. ANTs nonlinear registration to an in-house standard atlas was used to localize regions on T1-SST (a standard cortical target and seven candidate reference regions) for SUVR calculations. Serial PiB scans were coregistered using group-wise rigid registration with SPM12 to produce a mean-space PiB single-subject template image (PET-SST). A rigid registration between the PET-SST and the T1-SST was used to

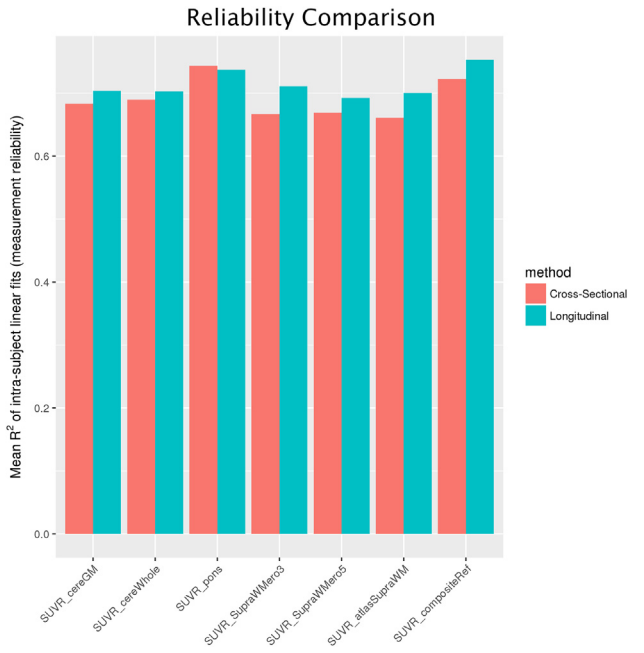

Figure 1. The reliability of intra-subject trajectories using the proposed longitudinal method was > that of the traditional cross-sectional method in 6/7 comparisons with varying reference regions.

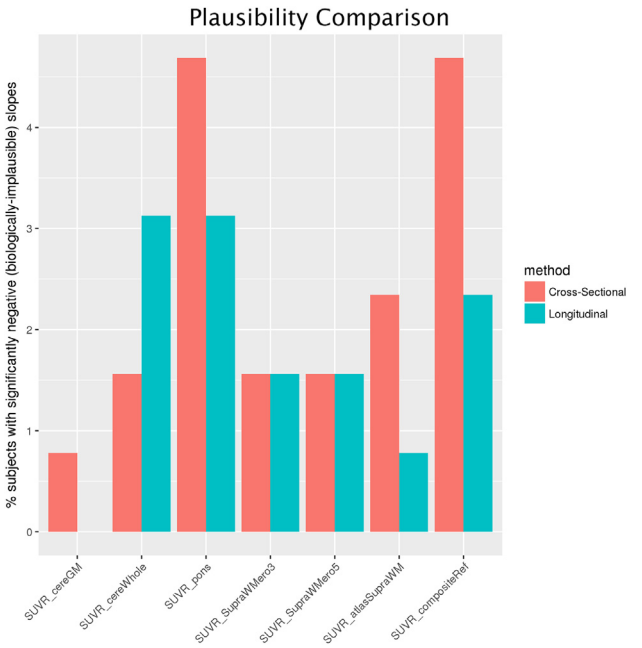

Figure 2. The percentage of subjects with biologically-implausible, significantly decreasing slopes using the proposed longitudinal method was ≤ that of the traditional method when using 6/7 tested reference regions.

Table 1
Reliability and plausibility performance for each combination of method and reference region

Method	Reference Region	Mean R^2 (reliability)	% Significantly Negative (implausible) slopes
Cross-Sectional	SUVR_cereGM	0.684	0.781
Longitudinal	SUVR_cereGM	0.704	**0.000**
Cross-Sectional	SUVR_cereWhole	0.690	1.563
Longitudinal	SUVR_cereWhole	0.703	3.125
Cross-Sectional	SUVR_pons	0.744	4.688
Longitudinal	SUVR_pons	0.737	3.125
Cross-Sectional	SUVR_SupraWMero3	0.667	1.563
Longitudinal	SUVR_SupraWMero3	0.711	1.563
Cross-Sectional	SUVR_SupraWMero5	0.669	1.563
Longitudinal	SUVR_SupraWMero5	0.692	1.563
Cross-Sectional	SUVR_atlasSupraWM	0.661	2.344
Longitudinal	SUVR_atlasSupraWM	0.700	0.781
Cross-Sectional	SUVR_compositeRef	0.723	4.688
Longitudinal	SUVR_compositeRef	**0.753**	2.344

B-spline resample each PET scan to the T1-SST space for each timepoint's SUVR calculation. We hypothesized that our approach (using a single mean-space T1-weighted image for segmentation and region localization, and a groupwise alignment of PET images with a single rigid registration to the mean-space T1) would yield improved longitudinal measurement performance compared to traditional intra-timepoint measurement methods. Our metrics of evaluation were: (1) reliability (larger $R^2$of linear intra-subject fits) and (2) plausibility (smaller percent of subjects with significantly negative slopes, indicating biologically-implausible decreasing amyloid) of intra-subject serial trajectories. We tested this hypothesis using scans of 128 Mayo Clinic study participants with 3 serial timepoints with MRI and PiB scans with baseline PiB SUVR $\leq$ 2.5 (and consequently expected non-decreasing amyloid trajectories). **Results:** Compared to the traditional cross-sectional method, the proposed longitudinal pipeline showed increased reliability of PiB-PET SUVR measures when using 6/7 tested reference regions. The percentage of subjects with biologically-implausible decreasing slopes using the longitudinal method was also $\leq$ that of the traditional method when using 6/7 tested reference regions. **Conclusions:** Our proposed automated longitudinal pipeline measuring PiB-PET SUVR by simultaneously processing serial scans produces measurements with improved reliability and plausibility compared to traditional intra-timepoint methods.

IC-P-020

RELATIONSHIP OF PHYSICAL ACTIVITIES DURING YOUNG ADULTHOOD AND MIDLIFE WITH BRAIN AMYLOID DEPOSITION, GLUCOSE METABOLISM, AND CORTICAL THICKNESS IN LATE LIFE

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Background: Epidemiological studies suggested that lifetime physical activities (PA) are related with the reduced risk of Alzheimer's disease (AD) dementia. However, very limited information is available for the association between PA during earlier lifetime and in vivo cerebral AD pathologies in late-life. This study aimed to investigate the relationship of PA in young adulthood and midlife with beta-amyloid (Aβ) accumulation and neurodegeneration in cognitive normal (CN) elderly individuals. **Methods:** One-hundred sixty five CN elderly subjects aged 61 years or over who participated in the Korean Brain Aging Study for Early Diagnosis and Prediction of Dementia (K-BASE) were included for this analysis. All the subjects underwent comprehensive clinical and neuropsychological assessment, ^{11}C-labelled Pittsburgh Compound B (PiB) positron emission tomography (PET), ^{18}F-fluorodeoxyglucose (FDG)PET, and magnetic resonance imaging. They also completed Lifetime Physical Activity Questionnaire (LTPAQ) for the measurement of PA during young adulthood (21-40) and midlife (41-60). PiB PET images were classified as Aβ positive if the mean PiB standard uptake value ratio (SUVR) was over 1.19 in one of the following regions: the frontal, lateral temporal, lateral parietal, and precuneus/posterior cingulate cortices(PC/PCC). In terms of neurodegeneration, hypometabolism positivity was defined as a mean FDG SUVR of AD-signature regions (the angular, PCC, and inferior temporal areas) $<$1.386, and cortical atrophy positivity was defined as a mean cortical thickness of AD-signature regions (the entorhinal, inferior temporal, middle temporal, and fusiform gyrus) $<$2.666 mm. **Results:** Among 165 participants, 42 participants classified as Aβ positive, 75 as hypometabolism positive, and 23 as cortical atrophypositive. Aβ positive group showed less PA during young adulthood (age 21-40) than Aβ negative group. Among various types of PA, only leisure activity level was higher in Aβ positive group than negative group. PA level during any lifetime period did not show difference between hypometabolism positive and negative group, or between cortical atrophy positive and negative group. **Conclusions:** Our results suggest that the higher PA during young adulthood, leisure activity in particular, may contribute to the delay of the development of AD by reducing amyloid deposition.

Table 1
Demographic data and LTPAQ (age$\geq$ 61, cognitive normal elderly) (n = 165)

Variables	Total (n = 165)	Amyloid (-) n=123	Amyloid (+) n=42	P value	FDGPET3roi(-) n=90	FDGPET3roi(+) n=75	P value	GM (-)n = 142	GM (+)n=23	P value
Age (years)	71.44(6.28)	**70.72(5.88)**	**73.57(6.98)**	**0.011**	70.91(5.88)	72.08(6.71)	0.235	**70.64(6.01)**	**76.39(5.76)**	**$<$0.001**
Education (years)	11.40(4.73)	11.37(4.52)	11.48(5.36)	0.904	11.51(4.76)	11.27(4.72)	0.742	11.57(4.60)	1035(5.44)	0.251
Sex (F/M)	85/81	64/59	21/21	0.859	47/43	38/37	0.877	77/65	8/15	0.115
APOEe4 (-/+)	133/32	123/42	32/10	0.498	74/16	59/16	0.693	114/28	19/4	1.000
LTPAQ										
21-40	106.37(100.69)	**114.62(104.43)**	**82.22(85.44)**	**0.072**	102.44(101.54)	11.09(100.13)	0.584	102.60(98.75)	129.66(111.43)	0.233
41-60	137.87(109.58)	142.46(110.39)	124.40(107.33)	0.358	148.02(121.72)	125.68(92.28)	0.193	137.72(109.78)	138.77(110.80)	0.966
Total (21-60)	244.24(178.86)	257.09(179.36)	206.62(174.04)	0.115	250.46(191.07)	236.78(163.97)	0.626	240.33(175.82)	268.43(199.07)	0.486
Occupational	191.86(180.08)	201.43(181.43)	163.83(175.18)	0.244	197.60(193.01)	184.97(164.25)	0.655	185.22(174.60)	232.85(210.52)	0.241
Home	31.97(46.54)	33.07(50.37)	28.76(33.16)	0.606	29.92(46.63)	34.43(46.63)	0.537	33.83(47.76)	20.52(37.00)	0.204
leisure	20.18(26.63)	**22.59(28.72)**	**13.13(17.73)**	**0.013**	22.93(29.91)	16.88(21.81)	0.146	21.01(26.46)	15.06(27.71)	0.322

Mean (SD). Total education (min 0 max 21). P value by independent t-test. Sex, ApoE difference by chi square (2-tailed, Fisher). LTPAQ: (Strength*hr/wk).