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Financial Management Skills in Aging, MCI and Dementia: Cross Sectional Relationship to 18F-Florbetapir PET Cortical β-amyloid Deposition

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Abstract

BACKGROUND: There is a need to more fully characterize financial capacity losses in the preclinical and prodromal stages of Alzheimer's disease (AD) and their pathological substrates.

OBJECTIVES: To test the association between financial skills and cortical β-amyloid deposition in aging and subjects at risk for AD.

DESIGN: Cross-sectional analyses of data from the Alzheimer's Disease Neuroimaging Initiative (ADNI-3) study conducted across 50 plus sites in the US and Canada.

SETTING: Multicenter biomarker study.

PARTICIPANTS: 243 subjects (144 cognitively normal, 79 mild cognitive impairment [MCI], 20 mild AD).

MEASUREMENTS: 18F-Florbetapir brain PET scans to measure global cortical β-amyloid deposition (SUVr) and the Financial Capacity Instrument Short Form (FCI-SF) to evaluate an individual's financial skills in monetary calculation, financial concepts, checkbook/register usage, and bank statement usage. There are five sub scores and a total score (range of 0–74) with higher scores indicating better financial skill.

RESULTS: FCI-SF total score was significantly worse in MCI [Cohen's d= 0.9 (95%CI: 0.6-1.2)] and AD subjects [Cohen's d=3.1(CI: 2.5-3.7)] compared to normals. Domain scores and completion times also showed significant difference. Across all subjects, higher cortical β-amyloid SUVr was significantly associated with worse FCI-SF total score after co-varying for age, education, and cognitive score [Cohen's f2=0.751(CI: 0.5-1.1)]. In cognitively normal subjects, after covarying for age, gender, and education, higher β -amyloid PET SUVr was associated with longer task completion time [Cohen's f2=0.198(CI: 0.06-0.37)].

CONCLUSION: Using a multicenter study sample, we document that financial capacity is impaired in the prodromal and mild stages of AD and that such impairments are, in part, associated with the extent of cortical β-amyloid deposition. In normal aging, β-amyloid deposition is associated with slowing of financial tasks. These data confirm and extend prior research highlighting the utility of financial capacity assessments in at risk samples.

Key words: Preclinical Alzheimer's, financial capacity, amyloid PET

The rapid growth of both aging populations and Alzheimer's disease (AD) cases across the world has spurred renewed interest into studies of financial capacity in the early stages of dementia (1-6). Financial capacity generally refers to one's ability to handle his or her own money and make appropriate decisions relating to financial affairs. Older adults hold a disproportionate share of wealth in most countries – a phenomenon referred to as graying of wealth - and in the US alone it is estimated that older adults hold some $18 trillion dollars in assets (1, 7, 8). Elderly subjects, especially those that live alone or are trusting, are also frequent targets (and victims) of financial fraud scams (9).

The estimated 45 million cases of AD dementia worldwide are expected to triple in coming decades barring an effective disease modifying therapy. There is now increasing interest in detecting AD at earlier stages such as mild cognitive impairment (MCI) or preclinical AD (defined by pathological biomarkers and/or genetic risk) (5). While loss of financial skills has long been recognized as a feature of advancing AD (10), the lack of sensitive instruments, with both performance based and timed measures, may have limited the full characterization of subtle financial capacity losses in the preclinical and prodromal stages of AD (11). Most instruments assessing instrumental activities of daily living in AD do not assess financial capacity in a comprehensive or performance based manner (3, 11).

The Financial Capacity Instrument (FCI), was designed to more thoroughly assess dementia populations on their financial ability (12). Initial studies of the FCI, by Marson and colleagues who pioneered the instrument, demonstrated that impairments in most financial activities were evident even in mild AD (4), that specific financial skill deficits could discriminate stable MCI from those that progressed to AD (5), that the instrument is capable of longitudinal use in MCI patients (13), and that MRI measures of hippocampal or angular gyri volumes were associated with FCI scores after co-varying for age, gender and education (14, 15).

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The Financial Capacity Instrument Short Form (FCI-SF), a modified version of the original FCI, was designed as a shorter test with items sensitive to the early stages of AD and includes both performance based and timed measures of complex financial abilities (16, 17). Recent studies of the FCI-SF have reported the FCI-SF Total Score may discriminate normal older adults from MCI or AD as well as some cognitive screening measures (17). Based on these promising findings, the FCI-SF is being tested in several studies for its utility as a screening or prognostic measure.

18F-florbetapir brain PET scan is a validated and US FDA approved test to measure the accumulation of fibrillary cortical β-amyloid deposition, one of the pathological hallmarks of AD (18). Prior reviews of 18F-florbetapir brain PET have also documented its initial utility for predicting future cognitive decline in aging and MCI (19). It is now being used to select subjects for disease treatment trials. Studies also report that between 20-30% of asymptomatic elderly subjects in research studies may have a positive scan suggesting the presence of preclinical AD pathology and a potential adverse long-term prognosis (20). These data raise the urgency to study the association between cortical β-amyloid deposition and financial capacity.

The Alzheimer's Disease Neuroimaging Initiative (ADNI), conducted across 50 plus sites in the US and Canada, has provided new insights into the timeline of biomarker changes in aging, MCI and AD (21-23).

The aims of this study were to use ADNI-3 data to analyze the relationship between cortical β-amyloid deposition and financial capacity (both global and across specific domains) in the cohort as well as in patient group and asymptomatic subjects. We also examined if FCI-SF scores would differentiate normal controls, MCI and AD (to confirm prior findings).

Methods

Study Design and Consent

Data used in the preparation of this article were obtained from the Alzheimer's disease Neuroimaging Initiative-3 (ADNI-3) (adni.loni.ucla.edu). ADNI was launched in 2003 with the third installment (ADNI-3) starting in 2016. The primary goal is to determine the relationships among genetic, biomarker, imaging, cognitive, and clinical testing across the entire spectrum of Alzheimer's disease as it progresses from a preclinical stage to dementia. ADNI-3 (ClinicalTrials.gov identifier: NCT02854033) involves 59 North American sites and study participants across three cohorts: normal controls (NC), mild cognitive impairment (MCI) and AD. Details of protocols and methods can be found online using the study manual [www.adni-info.org, http://adni.loni.usc.edu/adni-3/] (24).

The institutional review board at Duke University Health System and at each ADNI site reviewed and approved the ADNI protocol. All subjects and their legal representatives, where appropriate, gave written informed consent prior to data collection.

Participants

The data used for these analyses were summarized from the ADNI-3 database as of October 17, 2018. Participants were grouped at their baseline as either cognitively normal (NC), mild cognitive impairment (MCI) or to have mild probable AD dementia (AD). All participants were between the ages of 55-90 and assigned a diagnosis based on subject and informant histories, neurocognitive testing scores, laboratory tests, physical exams, brain MRI, the Clinical Dementia Rating (CDR) and physician judgment. Normal subjects could have a subjective memory complaint, but must score within normal parameters on the Wechsler Memory Scale Logical Memory II (WMS-II) and have a 0.0 on the CDR Global Rating. MCI subjects are required to have a subjective memory complaint, an objective memory deficit documented by the WMS-II, a CDR Global Rating of equal to or less than 0.5, and to not meet the criteria for AD. AD subjects have a subjective memory complaint, a larger deficit documented by the WMS-II, an MMSE score between 20-24, a CDR global score of 0.5 or 1.0, and a probability of AD. Additionally, participants with scores higher than 6 on the Geriatric Depression Scale (GDS) were excluded from the study. Details of diagnosis criteria are available through the ADNI-3 protocol [http://adni.loni.usc.edu/methods/documents/] (24). Both new and rollover ADNI-3 subjects with demographic information, a recorded MMSE, FCI-SF, and 18-F florbetapir β-amyloid PET global SUVr were considered for inclusion. Cognitively normal subjects had to have a Mini Mental State Exam (MMSE) of 25 or greater. Details of these tests and standardization across sites are available elsewhere (www.adni-info.org).

PET imaging

Global cortical β-amyloid deposition was measured in ADNI-3 using 18F-florbetapir amyloid PET imaging which was required for new enrollees and highly encouraged for rollover subjects. Details of scan techniques, standardization, quality control and calculation of SUVrs are reported elsewhere (http://adni.loni.usc.edu/methods/pet-analysis-method/pet-analysis/). The global SUVr averages signals across cortical regions typically affected in AD with higher SUVr indicating greater cortical β-amyloid deposition. Freesurfer processing is used to extract florbetapir means from grey matter within 4 regions (frontal, anterior/posterior cingulate, lateral parietal, lateral temporal)

Table 1. Baseline Demographic and Clinical Assessments by Diagnostic Group (mean ± SD)

	Control	MCI	AD
N	144	79	20
Age, y	71.61 ± 6.22	71.41 ± 6.74	74.84 ± 6.52 †‡
Gender, % female	52%	43%	45%
Education, y	16.83 ± 2.40	16.32 ± 2.78	15.45 ± 2.70 ‡
MMSE	29.14 ± 1.02	27.82 ± 2.35*	24.25 ± 3.57 †‡
18F-Florbetapir PET Global SUVr	1.13 ± 0.18	1.17 ± 0.25	1.43 ± 0.26 †‡

*MCI mean differs significantly from normal control means using 2-sample t-tests ($p < .05$) ; †AD mean differs significantly from MCI mean using 2-sample t-tests ($p < .05$); ‡AD mean differs significantly from normal control mean using 2-sample t-tests ($p < .05$)

and a reference region value is used to normalize the summary mean (25).

Financial Capacity Instrument –Short Form

The FCI-SF consists of 37 items that can evaluate an individual's financial skills in the domains of monetary calculation, financial concepts, register usage, and bank statement usage. There are five domain scores (i.e., Mental Calculation, Financial Conceptual Knowledge, Single Checkbook/Register Task, Complex Checkbook/Register Task, Using Bank Statement), and also a Total Score (range of 0–74), with higher scores indicating better financial capacity (16). The total score is a summary of the individual domains; Mental Calculation (0-4), Financial Conceptual Knowledge (0-8), Single Checkbook/Register Task (0-20), Complex Checkbook/Register Task (28), Bank Statement Management (0-14). Additionally, the FCI-SF considers Composite time during the grading of four specific tasks (i.e., medical deductible problem, simple income tax problem, single checkbook/register task, complex checkbook/register task) and includes two composite time scores for the two checkbook tasks and all timed tasks. Details of these tests and standardization across sites are available elsewhere (www.adni-info.org).

Statistical Methods

Demographic and cognitive variables were tested using analysis of variance (ANOVA) and t-tests. ANOVA and t-tests were also used to compare FCI-SF total score and subgroup scores between diagnostic groups. A multiple linear regression model was used to simultaneously estimate the effects of key baseline variables (gender, age, education, MMSE, β-amyloid SUVr) on FCI-SF Total Score as well as each FCI-SF domain. The significance threshold was set at .05 for our a-priori hypothesis. We also ran separate models in control and patient groups to examine the effect of β-amyloid in aging and memory impaired samples. A multivariate linear model was ran to analyze the direct relationship between the FCI-SF Total Score and β-amyloid SUVr. Lastly, we tested the effect of β-amyloid on specific FCI-SF domains. Our primary aim was to test whether greater β-amyloid deposition would be associated with lower financial capacity. To confirm prior findings we tested if FCI-SF scores would discriminate AD and MCI subjects from controls. Cohen's d and Cohen's f2 were used for estimating effect sizes. A Cohen's d effect of 0.5 is considered to be medium and >0.8 is considered a large effect. Cohen's f2 was used to estimate effect size between two continuous variables and a large effect is considered to be 0.4. All statistics were computed using R studio Version 1.1.463.

Results

Demographics

Table 1 displays demographic variables for the cognitively normal (n=144), MCI (n=79) and AD (n=20) subjects included in this study. AD subjects were significantly older than both the NC group and MCI group. AD subjects were also significantly less well educated than the NC groups. No significant gender difference was present between groups. As expected, t-tests showed that each group differed significantly in MMSE scores.

Effect of Diagnosis on Financial Capacity

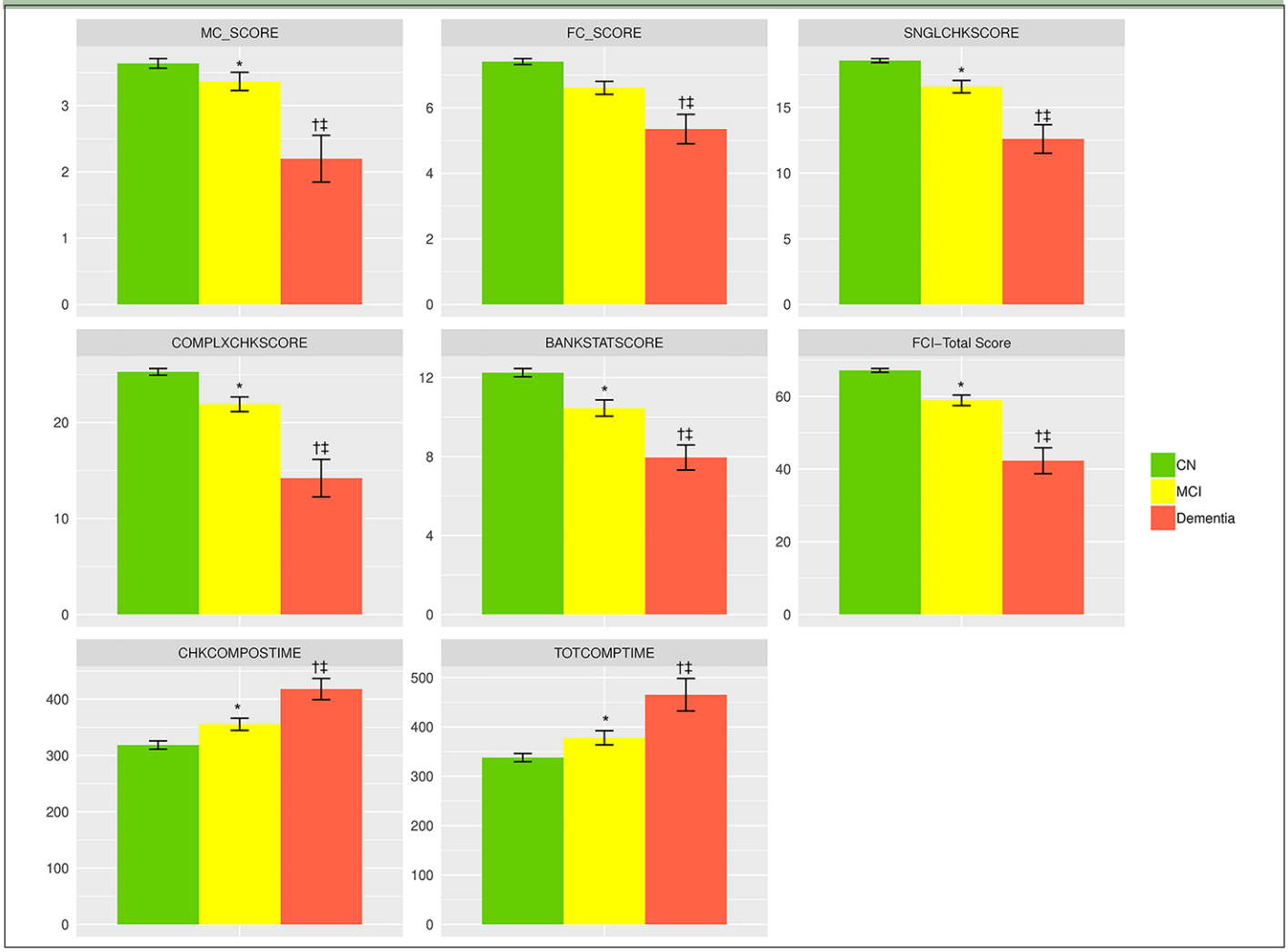
FCI-SF Total Score (mean ± SD) differed between NC (67.2 ± 6.18), MCI patients (58.9 ± 12.87) and AD patients (42.3 ± 15.96). ANOVAs showed the FCI-SF Total Score significantly differentiated all 3 diagnostic groups from one another ($p<.001$). ANOVAs showed that diagnostic groups differed significantly ($p<.0001$) on each domain; Mental Calculation , Financial Conceptual Knowledge, Single Checkbook/Register Task, Complex Checkbook/Register Task, Bank Statement Management, Check Composite Time, and Total Composite Time. Table 2 displays results of between group t-tests, which showed AD and MCI groups performed significantly worse than NC on FCI-SF Total Score and all domain scores (except the Mental Calculation domain score where the difference between the MCI and CN group did not reach significance). The effect size for AD versus NC

Table 2. FCI-SF Scores by Diagnostic Group (mean ± SD)

	Control	MCI	AD
N	144	79	20
FCI-SF Total Score (0-74)	67.15 ± 6.18	58.91 ± 12.87*	42.30 ± 15.96 †‡
Performance Domains			
Mental Calculation (0-4)	3.64 ± 0.87	3.37 ± 1.22	2.20 ± 1.58 †‡
Financial Conceptual Knowledge (0-8)	7.41 ± 1.09	6.61 ± 1.76*	5.35 ± 2.01 †‡
Single Checkbook/register (0-20)	18.57 ± 1.83	16.58 ± 4.20*	12.60 ± 4.86 †‡
Complex Checkbook/register (0-28)	25.28 ± 4.15	21.90 ± 6.79*	14.20 ± 8.73 †‡
Bank Statement Management (0-14)	12.25 ± 2.51	10.46 v 3.66*	7.95 ± 2.84 †‡
Time Components			
Checkbook/register Composite Time, s	318.37 ± 87.55	355.34 ± 95.38*	417.75 ± 84.08 †‡
Total Composite Time, s	337.89 ± 100.61	377.97 ± 128.11*	465.25 ± 146.89 †‡

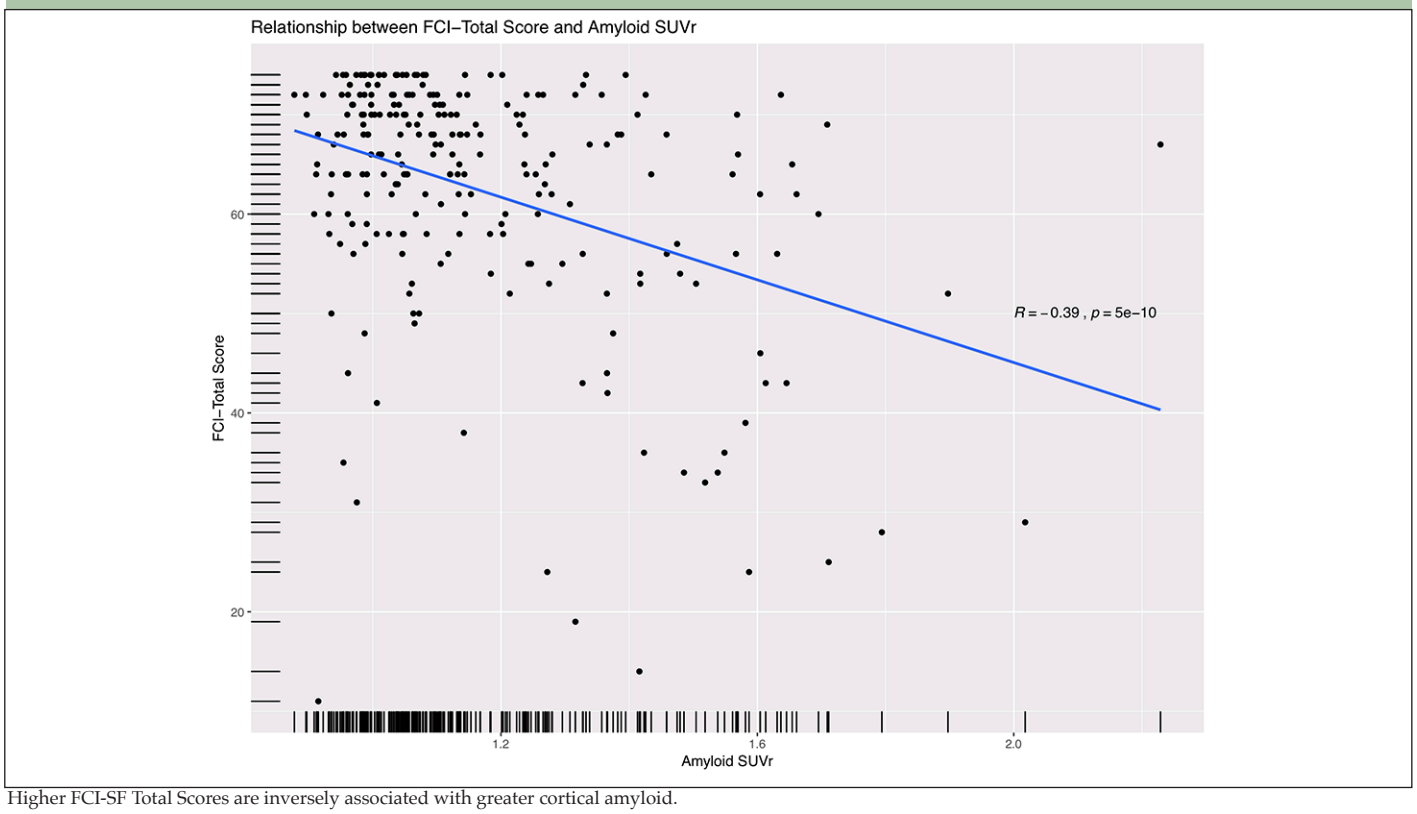
*MCI mean differs significantly from normal control means using 2-sample t-tests ($p < .05$); †AD mean differs significantly from MCI mean using 2-sample t-tests ($p < .05$); ‡AD mean differs significantly from normal control mean using 2-sample t-tests ($p < .05$)

Figure 1. FCI-SF Total and Items Score in Aging, MCI and AD



*MCI mean differs significantly from normal control means using 2-sample t-tests ($p < .05$); †AD mean differs significantly from MCI mean using 2-sample t-tests ($p < .05$); ‡AD mean differs significantly from normal control mean using 2-sample t-tests ($p < .05$)

Figure 2. Financial Capacity and Cortical ß-amyloid deposition in aging, MCI and AD



Higher FCI-SF Total Scores are inversely associated with greater cortical amyloid.

differences was large for the FCI Total Score [(d=3.1(CI: 2.5-3.7)] and all domain scores (d>1.1). The effect size for MCI versus NC was largest for the FCI-Total score [d=0.9(CI: 0.6-1.2)] followed by the two checkbook items (d=0.64) and medium for the completion time (d=0.36). Figure 1 shows FCI-SF scores by diagnosis.

Figure 3. Amyloid PET Images of Two Cases

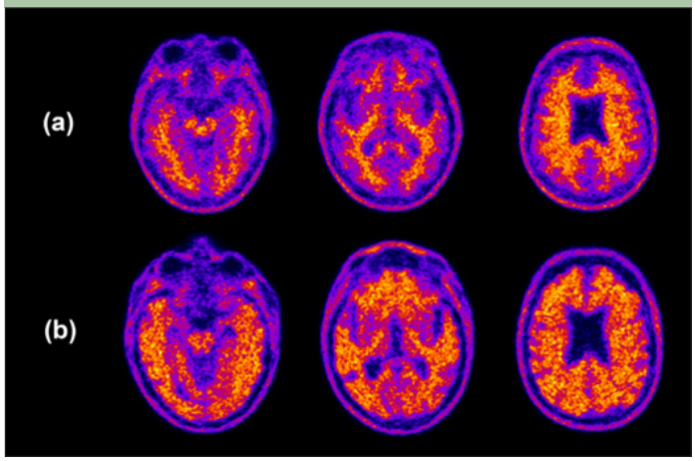


Figure 3a. 18F-Florbetapir PET image of a 74 year old normal control subject. PET scan is negative for β-amyloid. The subject had a normal financial capacity (FCI-SF Total Score=72); Figure 3b. 18F-florbetapir image of an 86 year old subject with mild Alzheimer's (MMSE=24). The PET scan is positive for β-amyloid. The subject had a significantly reduced financial capacity (FCI-SF Total Score=36).

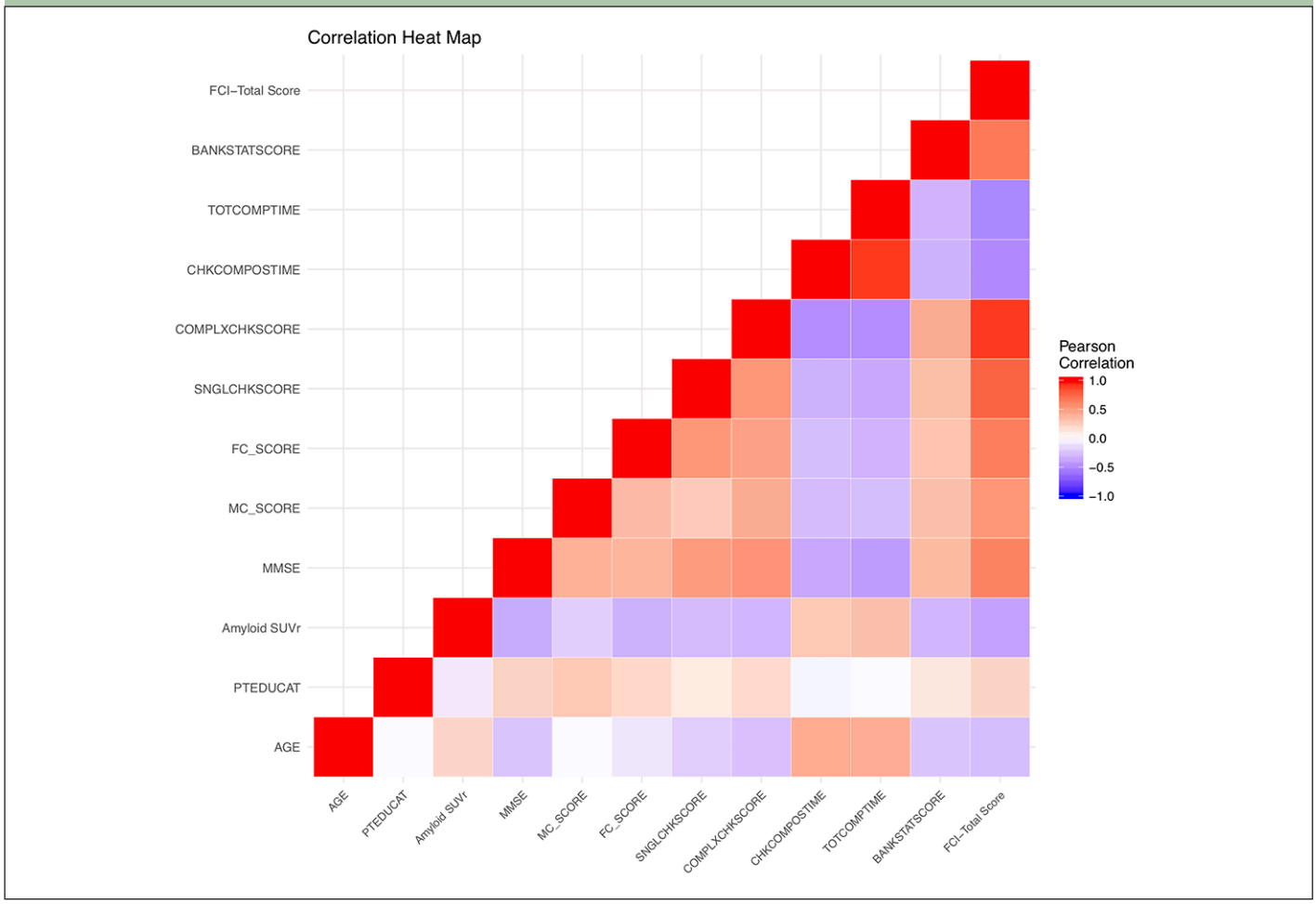
Effect of β-amyloid PET SUVr on FCI-SF Total Score

Figure 2 depicts the inverse relationship between lower FCI-SF Total Score and higher β-amyloid SUVr. Using an SUVr cut-off of 1.1, the effect size of β-amyloid positivity on lower FCI-SF total score was medium (d=0.55). Figure 3 illustrates color-rendered amyloid positive and negative PET scans from two subjects in ADNI-3 along with their financial capacity scores. After co-varying for age, education and gender, higher β-amyloid SUVr was associated with worse FCI-SF total score (p<.001) in the pooled sample. In this model, older age (p=.001) and lower education (p<.001) were also associated with worse FCI score but gender was not (p=.36). After co-varying for cognition as well (using the MMSE score), higher β-amyloid SUVr was still found to be associated with worse FCI-SF Total Score (p<.001) [Cohen's f2=0.75 (CI:0.51, 1.09)]. Older age (p=.04) and lower MMSE (p<.001) were also associated with worse FCI score in the pooled sample.

Relationship between β-amyloid SUVr and FCI-SF Subtest Domains

Multivariate linear regressions also show that higher β-amyloid SUVr was significantly associated with worse performance on all domains of the FCI-SF in the

Figure 4. Heat Map of Correlations Among Variables



pooled sample; Mental Calculation (p=0.007), Financial Conceptual Knowledge (p<.001), Single Check/Register (<.001), Bank Statement Management (p<.001), Complex Check/Register (p<.001), Check Composite Time (p<.001), and Total Composite Time (p<.001). Figure 4 is a heat map depicting the Pearson correlations between FCI-SF domains and β-amyloid SUVr with the significance and direction of correlation color coded.

Effect of β -amyloid PET SUVr on FCI-SF Scores in Cognitively Normal Older Adults

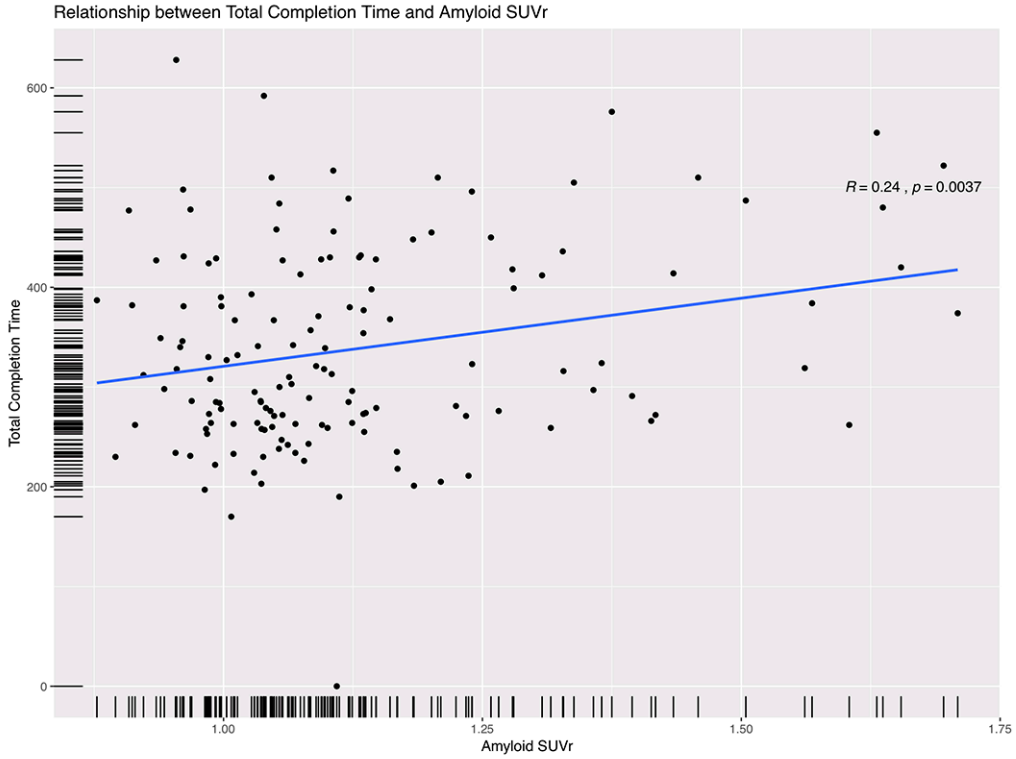
Simple linear regressions showed higher β-amyloid SUVr status was associated with slower Total Composite Time (p=.003) and Check Composite Time (p=.02), and worse Single Check/Register performance (p=.04) but other terms did not reach significance. Using an SUVr cut-off of 1.1, the effect size of β-amyloid positivity on slowing Total Completion Time was medium (f2=0.35). After co-varying for age, gender and education, higher β-amyloid SUVr was associated with slower Total Composite Time [Cohen's f2=0.198 (CI: 0.062-0.374)] (Figure 5) in normal older adults. After co-varying for age, gender and education, the effect of β-amyloid SUVr on FCI-SF Total Score failed to reach significance (p=.08). When cognition was added to this model, the effect of age on FCI-SF Total Score remained significant (p=.037) but the effects of β-amyloid SUVr, cognition, gender and education were not significant (p>0.05).

Discussion

We found the FCI-SF total score and all 5 domains as well as the completion time score were sensitive to detecting financial capacity impairments in both MCI and mild AD with large effect sizes. This confirms and extends prior findings (2, 4, 5, 6) to a sample from a multicenter ADNI setting. Overall, our study illustrates the feasibility and utility of administering the FCI-SF instrument across multiple raters and sites in the US and Canada and supports its utility and further development as a potential tool for assessing complex activities of daily living in MCI or AD in clinical trials.

Our study also found that cortical β-amyloid deposition had a significant effect on financial capacity. Furthermore β-amyloid load was linked with loss of skills on multiple financial domains such as mental calculation, conceptual knowledge, as well as handling checks and bank statements. This provides support that financial capacity may be more robustly associated with biomarker

Figure 5. FCI-SF Total Completion Time and PET Amyloid SUVr in Normal Controls



Total completion time was slower in normal control subjects with higher cortical amyloid.

defined MCI due to AD and β-amyloid positive AD dementia. It would be of interest to test whether disease modifying therapies impact financial capacity outcomes using the FCI-SF as a possible measure.

We also examined the links between cortical β-amyloid deposition and financial capacity declines in cognitively normal aging subjects. We found that a measure of financial quickness (total composite time) was adversely associated with increasing β-amyloid SUVr load and aging in normal subjects. The effect size for separating β-amyloid positive preclinical AD from amyloid negative controls on completion time was medium even with a relatively liberal SUVr cutoff for defining amyloid positivity. Our findings are consistent with a previous study (presented in abstract form) of FCI-SF scores in normal subjects from the Mayo Study of Aging which also found a significant effect of PIB-PET amyloid status on FCI completion time] (17). However, in our control sample, the effect of amyloid deposition on FCI-SF domains lost significance after co-varying for cognition.

The mechanisms underlying an association between amyloid deposition and financial capacity in aging and early dementia remain speculative since the neural circuits underlying financial capacity are not well understood. Prior studies have found associations between impaired financial skills and MRI measured angular gyrus volumes, hippocampal atrophy and white matter tract diffusivity (14, 26). Likewise, amyloid deposition has been associated with both functional and structural connectivity changes in preclinical and clinical AD (27, 28). Given the critical importance of white tract integrity to timed tasks, it is possible that alterations in white matter connectivity may underlie the links between amyloid and financial skills that we observed in our study. Further studies examining the relationship between FCI-SF and a variety of neuronal and pathological biomarkers may reveal additional insights.

Lastly, we found that there were no significant gender effects on FCI-SF score in normal aging or MCI subjects. This suggests the FCI-SF does not appear to have a significant gender bias in its raw scoring after adjusting for education effects. This supports the use of age and education adjusted norms for the FCI-SF (29).

There are some strengths and limitations to our study. ADNI-3 is a multisite study with participants in over 50 sites across the US and Canada. The careful and standardized protocol, entry criteria and rater training, and collection of amyloid PET data are the major strengths. As stated previously, the FCI-SF is a relatively well-studied and characterized tool. One weakness of our study is that our findings are cross-sectional and the sample studied from academic research centers may not be representative of the general population; hence the associations found should be viewed as preliminary warranting confirmation in longitudinal studies. The

effect sizes reported for the AD subjects must also be viewed with caution given the relatively small sample of AD subjects and their larger standard deviations. Further, while the FCI-SF is a promising tool, it has some potential disadvantages in that its relatively long, requires training of administration, and tools like "checks" may not be relevant to future generations. Lastly, our study cannot shed light on mechanisms underlying the association between amyloid and financial capacity and also cannot fully determine all such mediators that may underlie this effect. As data accumulates from ADNI-3 and other studies, such as the Brain Health registry and Mayo Study of Aging, some of these questions may be answered. Our findings thus should be viewed in that regard.

In summary, our study offers new insights into the links between pathological changes in the brain and financial capacity, a key functional activity essential for independent living. Our data also offers further guidance to researchers and clinicians on financial capacity changes in the early stages of preclinical and clinical AD dementia. We hope our findings serve to stimulate further research in this field which in turn may ultimately help clinicians to better monitor financial skills in at risk subjects and those with early dementia, and offer families timely advice to prevent financial adversity.

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Competing Financial Interests: MWW is the principal investigator for ADNI and all other authors are ADNI investigators at Duke. PMD is supported by NIH, DOD and Cure Alzheimer's Fund, has served as an advisor to and/or received grants from several companies and non-profits in this field, and owns stock in or serves on boards of companies whose products are not discussed here. Other co-authors may also have received grants or advisory fees from companies for other projects.

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Ethical standards: The institutional review board at Duke University Health System and at each ADNI site reviewed and approved the ADNI protocol. All subjects and their legal representatives, where appropriate, gave written informed consent prior to data collection.

Conflict of interest: We reported this under the existing para titled Competing Financial Interests.

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