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MRI Volume of the Medial Frontal Cortex Predicts Financial Capacity in Patients with Mild Alzheimer's Disease

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Abstract

Persons with mild Alzheimer's disease (AD) have significant deficits in financial abilities. This study examined the relationship between brain structure volumes, cognition, and financial capacity in patients with mild AD. Sixteen mild AD patients and 16 older adult comparisons completed the Financial Capacity Instrument (FCI), a psychometric measure of financial abilities, and also underwent magnetic resonance imaging (MRI) to obtain volumes of the bilateral hippocampi, angular gyri, precune, and medial and dorsolateral frontal cortices. Mild AD patients performed significantly below comparisons on the FCI and had significantly smaller hippocampi. Among mild AD patients, FCI performance was moderately correlated with frontal (medial and dorsolateral frontal cortex) and posterior (angular gyri and precune) cortical volumes. Stepwise regression demonstrated that medial frontal cortex volume predicted FCI score. The relationship between medial frontal cortex volume and overall FCI score was partially mediated by two measures of simple attention (DRS Attention, DRS Construction). The findings suggest that medial frontal cortex atrophy and associated declines in simple attention play an increasingly important role in declining financial skills in patients with mild AD.

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Keywords

Alzheimer's disease; financial capacity; magnetic resonance imaging; frontal cortex; precuneus; angular gyrus

Loss of instrumental activities of daily living (IADLs) (e.g., financial skills, medication management, food preparation, transportation) is a core early feature of dementia due to Alzheimer's disease (AD) (Gauthier et al. 1997). Loss of IADLs in AD increases dependence on others (Dodge et al. 2003), leads to substantial emotional (Kurz et al. 2003) and financial (Hill et al. 2006) costs, and ultimately is a harbinger for institutionalization (Andrieu et al. 2002). Decline in financial capacity is one of the earliest and most disruptive IADL changes in patients with mild AD (Lawton 1982). Financial capacity comprises a broad range of conceptual, pragmatic, and judgment abilities, ranging from basic (e.g. identifying and counting coins and currency) to more complex skills (e.g. paying bills, managing a bank statement, and exercising financial judgment) (Marson et al. 2000).

Our group has previously investigated financial capacity deficits in patients with AD using the Financial Capacity Instrument (FCI), a conceptually based, direct assessment measure of financial capacity (H.R. Griffith et al. 2003; Marson et al. 2000). Our studies using the FCI have shown that impairment of financial capacity first emerges in mild cognitive impairment (MCI), is already widespread in patients with mild AD, and is advanced and global in patients with moderate AD (Griffith et al., 2003; Marson et al., 2000; Triebel 2009). These deficits in FCI performance appear primarily to reflect the progressive cognitive changes characteristic of AD. Neurocognitive predictors of FCI performance in mild AD patients have included attention, written arithmetic skills, short-term memory, and visuomotor tracking abilities (Earnst et al. 2001).

The identification of such neurocognitive predictors raises the issue of the underlying neuropathology associated with declining financial capacity in AD. For example, the importance of attention to financial abilities suggests the salience of pathology within the midline cortical regions such as the posterior cingulate/precuneus and medial superior frontal cortex (Hao et al. 2005; Pardo et al. 2007; Lockwood et al. 2007; Small et al. 2003; H. R. Griffith et al. 2007). The dorsolateral frontal cortex may be involved in aspects of financial abilities related to decision-making, working memory, and the executive control of attention (Miller & Cohen, 2001). Lateral parietal regions such as the angular gyri are also important to financial capacity given their role in calculation, arithmetic knowledge, and visual attention (Hao et al. 2005). The prominence of hippocampal and medial temporal lobe pathology in AD (Jack et al. 2000) suggests that atrophy in these areas might also contribute to financial deficits in AD via disrupted episodic memory function (Sherod et al., 2009).

Despite advances in neuroimaging and in measurement of IADLs, there is currently an important knowledge gap concerning the interrelationships of brain volumetric changes, associated cognitive decline, and IADL impairment in neurodegenerative diseases like AD (H. R. Griffith et al. 2010). To date only a handful of studies have used neuroimaging to examine how brain changes in AD may be associated with decline in everyday functional abilities (Cahn-Weiner et al. 2007; Salmon et al. 2005; Antuono et al. 2001; H. R. Griffith et al. 2007). Such studies have generally relied on informant report of IADLs rather than standardized direct performance measures like the FCI. This is a potentially significant methodological weakness given that informant report can lack precision and that studies have suggested that patient and informant ratings of IADLs may be unreliable (Wadley et al. 2003; Loewenstein et al. 2001).

Our own group recently conducted a neuroimaging study of financial capacity using the standardized data available through the FCI. We found that decreased financial capacity in patients with amnesic MCI, often the transition phase between normal cognitive aging and AD, was associated with MRI volume of the angular gyri and written arithmetic skills, but not the hippocampi or short-term memory function (H. R. Griffith et al. 2010). This study was perhaps the first to link volume change in a specific neuroanatomical area (angular gyrus) and associated impairment in written arithmetic skills to diminished financial skills in patients with prodromal AD.

The current study sought to build on the above Griffith et al. (H. R. Griffith et al. 2010) study by investigating brain volumetric changes and financial capacity in patients with mild AD. Structural MRI volumetrics is an ideal method for examining brain-IADL changes in mild AD as it is sensitive to atrophy in mild AD (Jack et al. 2000), correlates with cognitive functioning in mild AD (Deweert et al. 1995), and has good correspondence with AD pathology at autopsy (Jack et al. 2002; Jagust et al. 2008). In the current study, we investigated MRI volumetrics of five brain structures suspected to play a role in financial abilities of persons with mild AD: medial prefrontal cortex, dorsolateral frontal cortex, medial parietal/precuneus, angular gyri, and hippocampi. As discussed above, these structures were chosen because they are brain regions affected in mild AD (Chetelat et al., 2002; Jack et al., 2000; Scihill, Schott, Stevens, Rossor, & Fox, 2002) and because of their prior association with cognitive abilities that likely support financial abilities measured by the FCI (Sherod et al., 2009). We also tested whether the relationship between MRI brain volumes and FCI performance in mild AD patients was mediated by cognitive abilities measured by the Dementia Rating Scale-2 (DRS-2) (Mattis, 1988).

Methods

Participants

Participants consisted of 16 patients with mild AD and 16 healthy older adult comparisons. Patients with mild AD were community-dwelling older adults who presented for clinical evaluation to the University of Alabama at Birmingham (UAB) Memory Disorders Clinic, a tertiary care outpatient clinic. They were subsequently referred to the UAB Alzheimer's Disease Research Center (ADRC) and an associated NIH funded study of functional change in MCI and mild AD (Cognitive Observations in Seniors (COINS)). All participants underwent a research assessment comprised of neurological evaluation, neuropsychological testing, brain MRI, and laboratory blood work. The diagnosis of mild AD was made in a consensus diagnostic conference using NINCDS/ADRDA criteria (Blacker et al. 1994; McKhann et al. 1984). Exclusion criteria for the mild AD group included evidence of another neurodegenerative disease, history of stroke, another chronic debilitating neurological illness (e.g., multiple sclerosis), severe organ disease, autoimmune disease, cancer (except skin cancer), alcoholism, or a terminal condition with less than 12 months to live. Participants were also excluded if they had untreated major depression or any other severe psychiatric disorder.

Comparison participants were 16 older adult volunteers recruited from the community through newspaper advertisements or health fairs and were selected such that there would be no group differences in age, education, race, or gender. These participants also underwent brain MRI and neurological and neuropsychological evaluation at the ADRC and were characterized as cognitively normal following ADRC diagnostic consensus conference. Comparison participants met the exclusion criteria listed above for participants with mild AD. Comparison participants were included in the current study in order to test for diminished brain volumes, impaired neuropsychological test scores, and impaired FCI scores in the mild AD group.

All study procedures were approved by the UAB Institutional Review Board.

Financial Capacity Instrument (FCI)

The FCI is a standardized psychometric instrument developed to directly assess the financial abilities of older adults (Marson et al. 2000). The FCI assesses financial abilities based upon a three-level conceptual model of the financial capacity construct: specific financial abilities (18 tasks); broader financial activities (9 domains); and overall financial capacity (Marson et al. 2000; H.R. Griffith et al. 2003). The development, reliability, and validation of the instrument have been described elsewhere (Marson et al. 2000). Participants were administered the FCI by a trained technician who scored performance using standardized criteria. In this study, only the FCI domains of *financial conceptual knowledge* (Domain 2), *bank statement management* (Domain 5), *financial judgment* (Domain 6), and *bill payment* (Domain 7) were used, as these represent some of the most sensitive areas of early financial dysfunction (Okonkwo et al. 2006). Participants' scores on these four domains were summed to create an abbreviated FCI Total Score.

The premorbid experience of our participants with the financial skills measured by the FCI was determined by self-report and/or informant report. This information was then used to correct for lack of prior experience in any applicable financial tasks and domains following our previously described method (H.R. Griffith et al. 2003).

Cognitive Tests

Global cognitive status was assessed through performance on the Mini-Mental State Examination (MMSE) (Folstein et al. 1975) and the total score of the Dementia Rating Scale-2 (DRS-2) (Mattis 1988). Simple attention was assessed via the DRS-2 Attention subscale (Mattis, 1988) and the DRS-2 Construction subscale (Mattis, 1988; Jurica, Leitten, & Mattis, 2001). Although the latter is labeled a constructional measure, studies have demonstrated that scores on the DRS-2 Construction subscale are also highly correlated with attention measures (Marson et al., 1997; also see Bobholz & Brandt, 1993). Memory was assessed with the DRS-2 Memory subscale and executive functioning was assessed with the DRS-2 Conceptualization and Initiation/Perseveration subscales (Mattis, 1988; Jurica, Leitten, & Mattis, 2001).

MRI Acquisition and Data Processing

MRI images were obtained using a Philips Intera 3Tesla MRI system with a quadrature TR head coil to measure gray matter volumes from our five regions of interest (ROI). These imaging sequences consisted of (1) multi-slice sagittal, axial, and coronal T1 FFE scout sequences acquired using TR/TE=11.1/4.6 ms, 256 × 128 resolution, and 10 mm slice thickness (for the purpose of image alignment) and (2) multi-slice sagittal T1 FFE acquired using TR/TE=9.3/4.6 ms, 240 × 240 resolution, and 2 mm slice thickness.

After the MRI images were obtained, they were transferred to a workstation running Statistical Parametric Mapping, Version 5 (SPM5; www.fil.ion.ucl.ac.uk/spm/software/spm5). Tissue segmentation was derived in SPM5 and involved segmentation/normalization of the brain and smoothing of the resulting gray and white matter images (Ashburner and Friston 2005). The T1 image set was first skull stripped and the origin of each scan manually set to the anterior commissure. A combined normalization/segmentation process was implemented using the prior probability templates provided with the SPM5 program. These tissue probability maps are modified versions of the International Consortium for Brain Mapping (ICBM) Tissue Probabilistic Atlases. The results of this segmentation/normalization process were gray matter, white matter, and cerebrospinal fluid images for

each subject normalized to the same stereotactic space. Finally, gray and white matter images were smoothed using an 8mm Gaussian kernel.

The five ROIs were then identified using the Wake Forest University (WFU) Pick Atlas (Maldjian et al., 2003, 2004) in SPM5. This method is based upon an anatomical parcellation of the Montreal Neurological Institute (MNI) MRI single-subject brain (Tzourio-Mazoyer et al. 2002) and has the advantage of requiring no trained user interface to reliably obtain volumetric masks from cortical and subcortical ROI after MRI images are segmented and normalized in SPM5. Similar methods have been shown to have good reliability with manual traces of the hippocampus in patients with dementia (Firbank et al. 2007). Based upon this method, we derived bilateral volumes of the following ROI (see Figure 1):

Superior/Medial Frontal Gyri - this region was defined on the medial aspect of the frontal cortex and included all of the superior frontal gyrus to a posterior border of the supplementary motor area and cingulate, with an inferior border at the line of the anterior-posterior commissure, at which point the orbital portion of the superior frontal gyri occurs (Tzourio-Mazoyer et al. 2002).

Middle Frontal Gyri - this region was defined on the dorsolateral aspect of the frontal cortex and included all of the middle frontal gyrus with a posterior border at the precentral sulcus, an inferior border at the middle frontal sulcus, and a superior and internal border at the superior frontal sulcus (Tzourio-Mazoyer et al., 2002).

Hippocampi - this region consisted of the gray matter in the region of the temporal ventricular horns including the dentate gyrus, uncus, and hippocampus proper, limited caudally by the parahippocampal ramus of the collateral fissure (Tzourio-Mazoyer et al. 2002).

Precunei - this region is defined on the medial cortical surface of both hemispheres with posterior boundaries of the parietooccipital sulcus, dorsally by the marginal sulcus, and ventrally by the subparietal sulcus (Tzourio-Mazoyer et al. 2002).

Angular Gyri - this region was defined anteriorly by the angular sulcus and caudally at the occipitoparietal line (Tzourio-Mazoyer et al. 2002).

The five ROIs were derived for both hemispheres. Given that asymmetries were not observed in these structures at the group level (i.e., homologous structures were highly correlated), hemispheric ROI volumes were summed to obtain bilateral ROI volumes, a procedure that also effectively reduced the number of statistical tests performed.

Statistical Analyses

Mild AD vs. Comparison Group—Demographic data were compared using independent samples *t* tests or Chi-square (for categorical data). Group differences on mental status, FCI, and MRI measures were tested using independent samples *t* tests. For all comparisons resulting in unequal variances between mild AD and control groups (Levene's Test: $p = .05$), we reported a *p* value that does not assume equality of variances.

Mild AD Group Only—Within the mild AD patient group, our primary group of interest, we first ran Pearson correlations to examine the associations among cognitive test scores, MRI volumes, and FCI score. We then performed a forward stepwise multiple regression (probability of *F* to enter = .05; probability of *F* to remove = .10) to determine which MRI volumes, if any, were particularly strong predictors of FCI score. Finally, to examine

potential cognitive mediators, we first identified those cognitive measures that were significantly correlated with both the predictor (MRI volume) and outcome (FCI score), in accordance with Baron & Kenney's (R. M. Baron and Kenny 1986) prerequisites for mediation. After identification of these cognitive measures, mediation models were tested using the Sobel method (MacKinnon et al. 2002; Sobel 1982). A two-tailed alpha level of .05 was adopted for all analyses. We also tested the mediation effects using a bias-corrected bootstrapping method (90% confidence intervals, 5,000 bootstrap resamples), which may have advantages compared to the Sobel test in cases where data are nonnormal (SPSS 'indirect' macro: www.afhayes.com; (Preacher and Hayes 2008).

Results

Mild AD vs. Comparison Groups

Demographics, Dementia Staging, and Clinical Characteristics—Demographics, dementia staging, and clinical characteristics are presented in Table 1. As expected, our samples showed no significant differences in terms of age, education, race, or gender. Staging using the Clinical Dementia Rating (CDR) (Morris 1993) scale revealed that all mild AD patients had CDR scores = 0.5 or 1, and all comparison participants had CDR scores = 0. As expected, the mild AD patients performed significantly below comparison participants on the MMSE ($P < .001$) and DRS-2 Total score ($P < .001$). In addition, the mild AD patients performed worse on the DRS-2 Initiation/Perseveration and Memory subtests ($P < .001$). They also showed a trend towards worse performance on DRS-2 Attention ($P = .056$) and Conceptualization ($P = .083$) subscale scores. Almost two thirds (63%) of the mild AD patients were taking a cholinesterase inhibitor for memory loss.

Financial Performance—There was a group difference in the abbreviated FCI Total Score with mild AD patients performing significantly worse than comparison participants ($P = .001$) (see Table 1).

MRI Volumes—MRI volumes from the five ROIs are displayed in Table 2. The hippocampi were significantly smaller bilaterally in mild AD patients compared to comparison participants ($P < .001$). There were no other significant volumetric differences (all P 's $> .05$).

Mild AD Group Only

Correlations: Cognitive Tests, MRI Volumes, and FCI Total Score—Table 3 shows the correlations among the cognitive measures, MRI volumes, and the FCI Total Score within the mild AD group. MRI volumes were generally moderately to strongly correlated with each other (r values ranging from .65 to .94). The medial frontal cortex volume was correlated with the DRS-2 Attention and Construction subscale scores (all P 's $< .05$). The correlations between cognitive measures and the dorsolateral frontal cortex, precune, angular gyri, and hippocampi volumes were not significant.

The FCI Total score was correlated with the DRS-2 Total score, and the DRS-2 Attention, Construction, and Conceptualization subscale scores (all P 's $< .005$). The FCI Total score was also correlated with volumes of the medial frontal cortex (see Figure 2), dorsolateral frontal cortex, precune, and the angular gyri (all P 's $< .05$), but not the hippocampi ($P > .05$).

The DRS-2 Total score and MMSE did not correlate with each other or any of the MRI volumes ($P > .05$; however, r values ranged from .33 to .49 for the correlations between the DRS-2 Total score and MRI volumes).

Regression Model: MRI Volumes and FCI Total Score—A stepwise regression model was used to determine the key MRI volume predictors of FCI Total score in mild AD patients, with all five ROIs entered into the regression model to assess significance. The medial frontal cortex ROI was the only brain volume that met inclusion criteria for the regression model, and it accounted for 34% of the variance in FCI Total scores ($F(1, 14) = 7.11, P = .018$).

Mediation Model: MFC Volumes, FCI Total Score, and DRS-2 Attention and Construction—The proposed mediation model is presented in Figure 3. This model tested whether the relationship between medial frontal cortex volume and FCI Total score (path c') was mediated by the DRS-2 Attention subscale score, the DRS-2 Construction subscale score, or both scores. As reported above, medial frontal cortex volumes correlated with DRS-2 Attention (path a1) and DRS-2 Construction (path a2) scores and, in turn, DRS-2 Attention and DRS-2 Construction scores were correlated with FCI Total score (paths b1 and b2, respectively). Thus, the initial criteria for mediation were met (R.M. Baron and Kenney 1986). The Sobel test statistic (2.09) was significant ($P = .037$) for the total effects when including both DRS-2 Attention and Construction scores as mediator variables in the model, indicating that the relationship of medial frontal cortex volume with FCI Total score (path c') was partially mediated by the DRS-2 Attention and Construction scores (direct effect: $t = 1.04, P = .320$). Neither DRS-2 Attention (indirect effect: $z = 1.55, P = .122$) nor Construction (indirect effect: $z = 1.10, P = .271$) scores alone were significant mediators of the relationship between medial frontal cortex volume with FCI Total score, and there was no significant difference in the pairwise contrast of Attention versus Construction scores as mediators (indirect effects: $P's > .05$). Bias-corrected confidence intervals further supported an indirect effect between medial frontal cortex volume with FCI Total score mediated by the DRS-2 Attention and Construction scores (90% CI = .58; 12.10) and confirmed there were no significant effects of either DRS-2 subscale scores alone (DRS-2 Attention: 90% CI = -.03; 10.80; DRS-2 Construction: 90% CI = -.59; 8.90).

Discussion

The present study investigated brain structure volumes in mild AD and their relationship to financial abilities in patients with mild AD. We found that MRI volumes of the frontal cortex (medial and dorsolateral frontal cortex) and posterior cortical regions (angular gyri and precunei) were moderately correlated with a direct performance measure of financial abilities (FCI) in patients with mild AD. A multivariate FCI predictor model demonstrated that medial frontal cortex volume was the strongest predictor of financial capacity, and this relationship was mediated by measures of simple attention (DRS-2 Attention and Construction subscales).

The study findings, coupled with our recently published work in amnesic MCI (H. R. Griffith et al. 2010), begin to suggest a trajectory of decline in financial capacity consistent with the neuropathological progression from amnesic MCI to mild AD (Scahill et al. 2002). Our group has previously found that brain metabolic changes in the precuneus/posterior cingulate, as measured by magnetic resonance spectroscopy (MRS), were associated with financial capacity impairments of patients with mild AD (H. R. Griffith et al. 2007). We also previously found that MRI volume of the angular gyri, but not volume of the medial frontal cortex, was associated with financial capacity impairments of patients with amnesic MCI (H. R. Griffith et al. 2010). In the current study, which involved a mild AD sample, we found posterior regions of the precunei and angular gyri continuing to play an important role in financial capacity, as reflected in their correlations with FCI performance. However, in the current study, only the midline frontal regions entered the multivariate FCI predictor model in mild AD. This finding appears consistent with the neuropathological course of AD,

which first and most prominently affects the medial temporal cortex (Jack et al. 2000) and posterior cortical regions (Chetelat et al. 2002), and then affects the frontal cortex as the disease progresses (Scahill et al. 2002), although we also found this appeared to be most true for midline vs. dorsolateral frontal regions. Our volumetric data generally correspond with this neuropathological course: hippocampal volumes were significantly smaller in the mild AD group compared to the age-matched comparison group, and while the other ROIs did not reach significance, they were smaller in the mild AD group compared to comparison group in all instances.

It is not surprising that we did not find a significant relationship between hippocampal volumes and financial capacity in our mild AD sample. Other authors have indicated that hippocampal volumes in patients with AD may fail to correspond with cognitive change as an artifact of the extensiveness of hippocampal atrophy (and loss of variability) and more widespread effects to other brain regions (Ridha et al. 2008). The severe hippocampal atrophy (-2 SD) evident in our patients may have limited the correlation of the hippocampus with financial abilities (e.g., due to range restriction). However, an alternative explanation to this is that the FCI, a laboratory administered measure, does not require a large episodic memory component as is normally needed in everyday (naturalistic) settings, and therefore would not be expected to correlate as strongly with hippocampal volume. Thus, the null hippocampal findings may speak to the specificity of the significant associations of FCI performance with volumes of the frontal cortex and posterior cortical regions.

This study's cognitive mediation model suggests that medial frontal cortex is a neural substrate for auditory and visual attentional abilities important to financial skills in patients with mild AD. FCI performance has previously been shown to be related to attention in AD patients (Earnst et al. 2001). The abbreviated FCI used in this study has tasks that include understanding and identifying information on bank statements and bills, understanding and applying financial concepts, conducting calculations, organizing bills for payment, and exercising financial judgment. A common aspect of these tasks in patients with AD appears to be whether the patients can still adequately attend to auditory and visual financial information presented in the task. For instance, a study of written arithmetic in patients with AD has demonstrated that these patients showed a variety of attentional and conceptual errors such as operation substitution and digit substitution (Martin et al. 2003). To the extent that similar errors can occur in performance on the financial tasks of the FCI, it is not surprising that the medial frontal cortex would share a relationship with financial abilities via attention. The medial frontal cortex has been implicated in attention (Mander et al. 2008; Hao et al. 2005; Pardo et al. 2007) and recently has been shown to have a role in regulation of everyday IADLs (Krueger et al. 2007). Thus, our findings are both consistent with our prior work in financial capacity as well as recent cognitive neuroscience findings regarding IADLs.

To our knowledge, the current study is one of the first to link specific structural brain and neurocognitive measures with direct IADL performance in patients with mild AD. The study builds on the findings of our prior MCI neuroimaging study (H. R. Griffith et al. 2010) by investigating, this time in a well-characterized mild AD group, interrelationships between multiple MRI volumes, cognitive function, and financial capacity - a specific key IADL. We note that few prior studies have investigated IADL performance in older adults using neuroimaging. In one study, MRI volumes of cortical gray matter and the hippocampus predicted clinician ratings of IADLs based upon caregiver interview in healthy individuals and patients with AD (Cahn-Weiner et al. 2007). Another study, using an informant-based rating of IADLs (The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)), examined the correspondence of ratings with hippocampal volume and white matter hyperintensities in a mixed group of English and Spanish speakers, some of whom

were cognitively impaired based upon psychometrically-defined thresholds (Farias et al. 2004). Both the present study and the earlier Griffith et al. (H. R. Griffith et al. 2010) study represent extensions of these prior reports, and support the premise that structural brain imaging (MRI volumetrics) is sensitive not only to cognitive impairments in prodromal and clinical AD, but also to “downstream” deficits in cognitively demanding IADLs such as financial capacity.

Limitations of the current study should be acknowledged. Although the brain volumes of interest and IADL measure (FCI) used were the same compared to our prior study examining FCI performance in MCI patients, we used a different set of cognitive mediators (H. R. Griffith et al. 2010). This precluded a comparison between cognitive mediators of FCI performance in the current AD sample and our prior MCI sample. This study also included a relatively small sample size. The magnitudes of the reported effects are quite large; however, replication of the findings within a larger sample is needed to confirm the precision of these estimates and the confidence that these effect sizes generalize to the larger population of individuals with mild AD. It should be noted that the current findings do not rule out the possibility that other regions contribute to FCI performance in mild AD. For example, a recent study reported that ventromedial prefrontal dysfunction was associated with increased credulity for misleading information in patients with adult-onset brain lesions (Asp et al.). The relationship between ventromedial cortex and other relevant structures (e.g., anterior cingulate cortex) with FCI performance warrants investigation. There also may be other important cognitive and IADL functions, not measured in the present study, linked to neuropathological changes associated with mild AD, which should be investigated in future replication studies.

In conclusion, financial abilities showed a robust relationship with volume of the medial frontal cortex, and this relationship was mediated by measures of simple attention. The current findings underscore the clinical significance of atrophy and neurodegeneration in areas outside of the medial temporal lobe in mild AD. They also hold promise for future investigations of IADL using conjoined neuroimaging and neuropsychological procedures.

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Figure 1.

Regions of interest masks (in red) used for volumetric analyses in SPM5 overlaid on a single subject MRI template in standard (MNI) space in the coronal (left column), sagittal (middle column), and axial (right column) views for the (a) medial frontal cortex, (b) precuneus, (c) dorsolateral frontal cortex, (d) angular gyrus, and (e) hippocampus.

Figure 2.

Scatterplot demonstrating the correlation ($r = .58$, $p < .05$) between the adjusted medial frontal cortex volumes (x-axis) and FCI Total scores (y-axis) in the mild AD group. Medial frontal cortex volumes were transformed to z scores based on the control group brain volume to enhance interpretability.

Figure 3.

Diagram of the proposed mediation model for the relationship between medial frontal cortex volume and financial capacity (FCI) mediated by attention (DRS-2 Attention and Construction) within the mild AD group.

Table 1

Demographics, Dementia Staging, & Clinical Characteristics between Groups

	Comparisons n = 16	Mild AD n = 16	P value
Age in years mean (SD)	75.00 (4.43)	76.94 (8.16)	n.s.
Sex (males / females)	5 / 11	7 / 9	n.s.
Race (Caucasian / African-American)	15 / 1	15 / 1	n.s.
Education in years mean (SD)	14.31 (2.75)	14.31 (2.47)	n.s.
MMSE mean (SD)	29.44 (0.73)	25.13 (1.82)	<.001
DRS-2 Total mean (SD)	137.44 (2.50)	118.44 (13.17)	<.001
DRS-2 Attention mean (SD)	35.44 (1.54)	33.81 (2.88)	.056 *
DRS-2 Initiation/Perseveration mean (SD)	36.38 (0.81)	29.75 (4.81)	<.001
DRS-2 Construction mean (SD)	5.75 (0.58)	5.38 (1.09)	n.s.
DRS-2 Conceptualization mean (SD)	36.25 (1.88)	33.94 (4.70)	.083 *
DRS-2 Memory mean (SD)	23.63 (0.96)	15.56 (2.90)	<.001
CDR Staging (0 / 0.5 / 1)	16 / 0 / 0	0 / 9 / 7	.001
Cholinesterase Inhibitor (yes/no)	0/16	10 / 6	---
Financial Capacity Instrument+ mean (SD)	124.75 (4.17)	96.69 (25.99)	.001

MMSE = Mini Mental Status Examination; DRS-2 = Dementia Rating Scale – 2

n.s. = not significant, $P > .10$;* $P < .10$

+Abbreviated FCI maximum score = 133.

Table 2

Region of Interest Volumes between Groups

	Comparisons n = 16 Mean (SD)	Mild AD n = 16 Mean (SD)	P value
Hippocampi	5.72 (0.51)	4.70 (0.75)	<.001
Medial Frontal Cortex	11.00 (1.37)	10.84 (1.74)	n.s.
Dorsolateral Frontal Cortex	22.96 (2.57)	22.44 (3.57)	n.s.
Precunei	16.59 (1.86)	16.10 (2.33)	n.s.
Angular Gyri	7.60 (0.96)	7.31 (1.05)	n.s.

n.s. = not significant, $P > .05$

Table 3

Correlations among Mental Status, MRI Volume ROIs, and FCI Total Score in Mild AD Patients

	DRS	ATTN	I/P	CONS	CONC	MEM	MFC	DFC	AG	PQ	HIP	FCI
DRS	---											
ATTN	.90**	---										
I/P	.81**	.70**	---									
CONS	.65**	.68**	.36	---								
CONC	.84**	.75**	.40	.76**	---							
MEM	.70**	.46	.52*	.06	.52*	---						
MFC	.49	.51*	.25	.51*	.48	.35	---					
DFC	.38	.39	.14	.40	.41	.29	.93**	---				
AG	.35	.36	.23	.41	.32	.15	.74**	.86**	---			
PQ	.40	.42	.35	.43	.31	.15	.76**	.86**	.94**	---		
HIP	.33	.40	.26	.31	.21	.22	.78**	.74**	.72**	.65**	---	
FCI	.73**	.75**	.44	.69**	.73**	.40	.58*	.51*	.55*	.53*	.26	---

* $P < .05$;

** $P < .01$

Note: AG = angular gyrus; ATTN = DRS-2 Attention; CONS = DRS-2 Construction; CONC = DRS-2 Concentration; DFC = dorsolateral frontal cortex; DRS = Dementia Rating Scale-2 Total score; FCI = Financial Capacity Instrument; HIP = hippocampus; I/P = DRS-2 Initiation/Perseveration; MEM = DRS-2 Memory; MFC = medial superior frontal cortex; PQ = precuneus.