

Background

Cardiovascular disease (CVD) remains a primary cause of mortality in the United States. It is a pervasive health problem that has tremendous psychosocial and economic cost.

Patients with CVD are at increased risk for stroke and other forms of cerebrovascular disease. Furthermore, there is significant overlap in the risk factors for both CVD and cerebrovascular disease. There is evidence that CVD can lead to insidious cerebrovascular changes that can lead to significant neurocognitive and functional changes, including vascular dementia.

Increasing evidence suggests that persons with CVD often experience neurocognitive impairment. CVD patients generally experience difficulty on task of executive function, psychomotor speed, and memory. Recent studies demonstrate that cognitive deficits vary as a function of CVD severity, with poorer health associated with the greatest impairment.

One possible explanation for this relationship that has not been examined is the possibility of changes in white matter integrity. Recent studies demonstrated fractional anisotropy (FA) measured using diffusion tensor imaging (DTI) is closely related to cognitive performance in persons with cerebrovascular disease.

The purpose of this study was to investigate the relationship between measures of FA, CVD severity, and cognition among a group of patients at increased risk for cerebrovascular disease.

Participants

Twelve patients (7 males and 5 females) were recruited from local medical centers and private practice with a history of cardiovascular disease. Patients were excluded who had any 1) neurological Disease, 2) chronic Intractable Psychiatric Disorder, 3) previous drug or alcohol abuse, 4) head injury (LOC>10 minutes), or 5) MRI Contraindications.

Patients demographics are included in Table 1 by gender.

The Framingham Stroke Risk Profile (FSRP) was used as a measure of disease severity.

Patients were also administered a neuropsychological battery of tests across a wide range of domains. For this study, only the results for the similarities, block design, coding, and digit span subtests from the Wechsler Adult Intelligence Scale—third edition (WAIS-III) are presented.

Table 1: Basic Patient Demographics

	AGE	EDU	MMSE	Cardiac Output	Ejection Fraction	Systolic BP	Diastolic BP
Males (n=7)	71.14 ± 8.53	15 ± 2.52	29.43 ± 0.54	3.86 ± 0.72	0.56 ± 0.13	132.81 ± 23.27	68.26 ± 10.31
Female (n=5)	75.4 ± 8.08	13 ± 2.58	28.4 ± 1.82	3.26 ± 0.60	0.67 ± 0.14	119.42 ± 5.47	57.06 ± 5.25

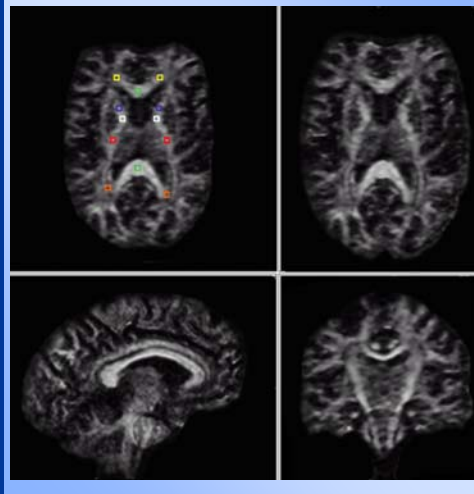
Methods

Imaging Protocol—We collected co-registered sagittal double spin-echo, echo-planar diffusion-weighted images as follows: 3 acquisitions with offset in slice direction by 0.0mm, 1.7mm and 3.4 mm, 5mm thick slices, 0.1mm inter-slice spacing, 30 slices per acquisition, 128x128 matrix, 21.7cm x 21.7cm FOV (by interleaving the three, we get true 1.7mm3 resolution images), TR=7200, TE=156. Diffusion gradients will be applied in 12 non-collinear diffusion directions with 2 b magnitudes: 0, 1000 mm/s², NEX=3. We used the Siemens' MDDW protocol with partial echos and with interpolation on. Time per acquisition = 4:48 min (x3 runs).

ROI analysis—We used a region of interest (ROI) method using ANALYZE 6.0®. FA maps were reoriented along the ACPC axis then registered with the T1 MPRAGE sequence for accurate placement of ROIs. ROIs were sampled in three adjacent axial slices where the caudate was at it widest width. Small 3 mm by 3 mm wide ROIs were placed in genu and splenium of the corpus callosum, right and left frontal forceps minor, right and left anterior limb of the internal capsule, right and left posterior limb of the internal capsule, the right and left genu of the internal capsule, and right and left (see Figure 1). We aggregated the measures by taking the average of the left and right measures. FA for each of the ROIs was back calculated using the scan parameters.

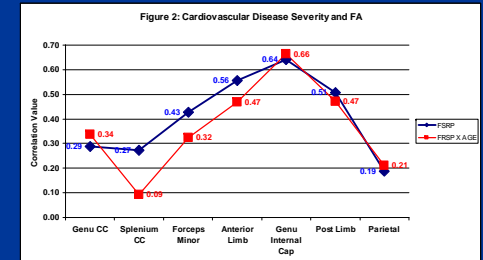
FSRP—The Framingham Stroke Risk Profile is a measure developed to estimate stroke potential in patients with established vascular disease. The measure incorporates age, systolic blood pressure, hx of hypertension treatment, diabetes, tobacco use, hx of CVD, atrial fibrillation, and left ventricular hypertrophy into a single measure of risk.

Figure 1: ROI Placement Illustration

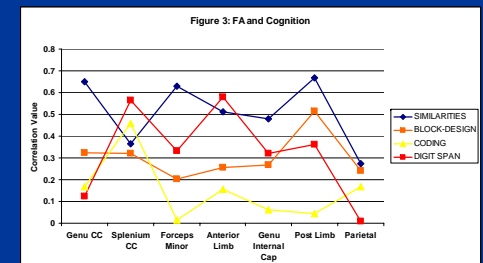


Results

There was a significant relationship between disease severity (FSRP) and measures of FA in the internal capsule ($p < 0.05$). This appears to be somewhat independent of age for most measures of FA in the ROI (see partial correlation results).



Preliminarily, we looked at the relationship between FA changes and four measures from the WAIS-III. Results demonstrated significant relationships for several measures and some possible dissociations between task demands and ROIs.



Summary and Conclusions

- These data suggests that FA varies as a function of CVD severity in older adults.
- The most significant relationships with CVD severity are found in the frontal subcortical areas of the internal capsule.
- This is consistent with the subcortical clinical picture often observed in patients with vascular type dementia.
- FA changes in these areas are likely to explain some of the common cognitive deficits observed in these patients, namely psychomotor slowing and speed of processing.
- These effects appear to be independent of age for most ROIs.
- CVD patients represent a "at-risk" group when studying the development of cerebrovascular disease and dementia.