Diffusion Tensor Imaging: Aging and Alcoholism

Adolf Pfefferbaum and Edith V. Sullivan
SRI International
Stanford University School of Medicine

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None

Adolf Pfefferbaum and Edith V. Sullivan
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Stanford University School of Medicine
Neuroscience Program
Brain-Behavior Relationships

MR Neuroimaging
- Structural MRI
- fMRI
- DTI
- Molecular Spectroscopy
- Postmortem MRI

Neuropsychology
- Executive Functions
- Components of Memory: declarative, procedural, working, remote, verbal, nonverbal
- Visuospatial Functions
- Motor Speed & Learning
- Gait & Balance

Name the color:
- BLUE
- GREEN
- YELLOW
White Matter Integrity
Age, Alcoholism, and Function

- Imaging brain white matter in normal aging
  - Macrostructural volumes
  - Microstructural constituents
  - Genetic contribution to structure

- White matter integrity and function in age

- White matter integrity and function in alcoholism

- White matter integrity and connectivity
Brain Development and Aging

Brain weight increases fourfold from birth to about 10 years of age

1 year old  18 year old  76 year old
Cortical Tissue Volumes

Gray Matter

White Matter

Pfefferbaum et al. Archives of Neurology 1994
The Normal Aging Brain

95 Normal Healthy Men

Cortical Sulci
Volume (cc)

Cortical Gray Matter

Cortical White Matter

Pfefferbaum et al. Archives of Neurology 1994
The Normal Aging Brain

54 Normal Healthy Women

Cortical Sulcal CSF
- $r = 0.62$, $p = 0.001$

Cortical Gray Matter
- $r = -0.68$, $p = 0.001$

Cortical White Matter
- $r = 0.15$, n.s.

Sullivan et al. Neurobiology of Aging 2004
Callosal vs. Ventricular Aging
Differential Rates of Change over 4 Years

- Annual ventricular expansion = 2.9%
- Annual callosal shrinkage = -0.9%

Change in size and morphology of the corpus callosum largely due to ventricular expansion

215 Men, age 70-82 years old

Sullivan et al. Cerebral Cortex 2005
MR Diffusion Tensor Imaging (DTI)

- Index of microstructural integrity (e.g., in white matter, myelin)
  - Intravoxel coherence: measures magnitude (diffusivity) and orientation (anisotropy) of freely diffusing water molecules within individual voxels

- Diffusivity Image (CSF brightest)
- Fractional Anisotropy Image (White matter brightest)

- Small macrostructural change in white matter volume with age
- Is there detectable microstructural change?
DTI Metrics

FA

MD

Axonal integrity

Myelin integrity

\( \lambda_L \)

\( \lambda_T \)
Normal Aging of White Matter

Microstructure: Partner MRI+DTI

31 yr old

71 yr old

Normal Aging
Corpus Callosum Microstructure

FA Image

- orientation of diffusion
- white matter brightest

Pfefferbaum et al. *Brain* 2007
Age Effect in the Anterior Corpus Callosum

Sullivan et al. NeuroReport 2000
Frontal Distribution
Age Effects on Supratentorial White Matter FA

Fractional Anisotropy (%)

left hemisphere
right hemisphere

10 younger
10 older

p-value

0.001
0.05

0 50 100 150 200

anterior slice (mm) posterior

genu AC PC splenium
Heritability of Callosal FA

14 MZ Twin Pairs

18 DZ Twin Pairs

Percent variance

Callosal size: 5:1
Splenium FA: 3:1
Genu FA: 1:1

Genetic (A) and Environmental (E)

Pfefferbaum, Sullivan, Carmelli NeuroReport 2001
Quantitative Fiber Tracking

- **Intravoxel coherence**: measures magnitude (diffusivity) and orientation (anisotropy) of freely diffusing water molecules within individual voxels.

  - **Diffusivity Image**: (CSF brightest)
  - **Fractional Anisotropy Image**: (White matter brightest)

  - FA in anatomically defined ROIs of corpus callosum

- **Intervoxel coherence**: measures anisotropy and diffusivity on a voxel-to-voxel basis for (quantitative) fiber tracking.

  - FA in **fibers** that course through defined ROIs of corpus callosum
Quantitative Fiber Tracking

- Identify fibers with a target and source model
- Compute FA and diffusivity along the entire fiber bundle, number of fibers, fiber length
- Examine central, proximal, and distal fiber bundle segments

» **Intervoxel coherence**: measures anisotropy and diffusivity on a voxel-to-voxel basis for (quantitative) fiber tracking

FA in **fibers** that course through defined ROIs of corpus callosum
Quantitative Fiber Tracking
Fibers Coursing through Corpus Callosum and Age

26 year old woman

73 year old woman

FA

ADC

% Fractional Anisotropy

Apparent Diffusion Coefficient

Sullivan et al.
Cerebral Cortex 2006
White Matter Systems and Performance
Pathways of Neural Communication

- **Projection fibers**
  - corticospinal tracts
  - pontocerebellar tracts
- **Commissures**
  - interhemispheric communication
- **Association fibers**
  - long fasciculi and short U-fibers
  - intrahemispheric communication
Quantitative Fiber Tracking
Age and Sex (N=120)

- Diffusivity is more sensitive than FA to age differences in several regions.

- Sex differences over age were seldom observed.

Sullivan, Rohlfing, Pfefferbaum *Neurobiology of Aging* 2010
Superior and Frontal fiber bundles were more vulnerable to age effects than inferior or posterior bundles.

In general, men and women showed similar regional age effects.
Neither age nor sex differences occurred in FA or diffusivity in pontine or cerebellar tracts.
Progression?
Progression over 2 Years?

- Fractional Anisotropy (FA)
- Apparent Diffusion Coefficient (ADC)

- Prefrontal, Premotor, Precentral, Postcentral, Temporal-Parietal

Sullivan, Rohlfing, Pfefferbaum, *Developmental Neuropsychology* 2010
Progression over 2 Years?

26 year old woman

80 year old woman

Sullivan, Rohlfing, Pfefferbaum Developmental Neuropsychology 2010
Progression over 2 Years?

Sullivan, Rohlfing, Pfefferbaum *Developmental Neuropsychology* 2010
Corpus Callosum and Age
Central vs. Lateral Fibers

Sullivan, Rohlfing, Pfefferbaum Developmental Neuropsychology 2010
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FA and Alternated Finger Tapping

Interhemispheric Transfer Test

Sullivan et al. *NeuroReport* 2000
Internal Capsule Sample and Age

Fine Finger Movement

**Internal Capsule**

- **FA**
  - Men: $r = -0.24$, $p = 0.0273$
  - Women: $r = -0.18$, $p = 0.15$

- **ADC**
  - Men: $r = 0.41$, $p = 0.002$
  - Women: $r = 0.39$, $p = 0.0015$

- **$\lambda_L$**
  - Men: $r = 0.29$, $p = 0.0314$
  - Women: $r = 0.32$, $p = 0.0103$

- **$\lambda_T$**
  - Men: $r = 0.40$, $p = 0.0028$
  - Women: $r = 0.37$, $p = 0.0023$

**Sullivan et al.**
*Neurobiology of Aging* 2010
Internal Capsule
Topological Organization

Anterior Limb
- frontopontine fibers
- corticothalamic fibers
- caudatoputamenal fibers

Genu (middle)
- corticobulbar fibers
- corticoreenticulobulbar fibers

Posterior Limb
- corticospinal fibers
- corticorubral fibers
- corticothalamic fibers
- thalamocortical fibers

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Internal Capsule Tracts
Fractional Anisotropy

Superior: Young > Elderly (p=.0006), no group x A-P interaction
Central: Young > Elderly (p=.0001), no group x A-P interaction
Inferior: Young > Elderly (p=.0001), no group x A-P interaction

Sullivan, Zahr, Rohlfing, Pfefferbaum
Neuropsychologia 2010
Internal Capsule Tracts
Transverse (λT) Diffusivity

Superior: Young < Elderly (p=.0001), no group x A-P interaction
Central: Young < Elderly (p=.0001), group x A-P interaction trend (p=.0917)
Inferior: Young < Elderly (p=.0001), no group x A-P interaction

Sullivan, Zahr, Rohlfing, Pfefferbaum
*Neuropsychologia* 2010
Internal Capsule and Performance
Fractional Anisotropy

Upper Limb

Fluencies

Damage to internal capsule
• amotivation to speak
• facial and lingual weakness

Sullivan, Zahr, Rohlfing, Pfefferbaum
Neuropsychologia 2010
Internal Capsule and Performance

Transverse (T) Diffusivity

Upper Limb

Fluencies

Sullivan, Zahr, Rohlfing, Pfefferbaum

Neuropsychologia 2010
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Alcohol Dependence: DSM-IV

- Maladaptive pattern of alcohol use, leading to clinically significant impairment or distress, manifested by 3 or more of the following in a 12-month period:

  - Tolerance
  - Withdrawal
  - Increasing consumption
  - Unsuccessful in cutting down
  - Inordinate time spent obtaining alcohol
  - Marked deterioration in life activities
  - Continued use despite physiological or psychological problems

12.5% men, 1.5% women lifetime prevalence of alcohol dependence
Alcoholism: Common and Costly

- 7 to 10% of U.S. adult population
- 14 to 20% of admissions to private hospitals
- 30 to 35% entering university or municipal teaching hospitals
- 50% of those being treated in VA medical, surgical, and psychiatric inpatient facilities

About 1/3 to 1/2 of treatment-seeking alcoholics have detectable cognitive or motor impairments.
Alcoholism and White Matter

- **In vivo studies**
  - White matter = gray matter volume shrinkage

- **Postmortem studies**
  - White matter more affected than gray matter
  - Demyelination
  - Microtubule disruption
  - Axonal deletion
  - Notable in frontal regions

⇒ **DTI quantification of FA and diffusivity components**
Alcoholism and White Matter FA

32 Control Men  
42 Control Women

40 Alcoholic Men  
17 Alcoholic Women

Pfefferbaum, Adalsteinsson & Sullivan  
*Biological Psychiatry*  2006
Age-Alcoholism Interaction

Callosal size

Callosal diffusivity

Pfefferbaum et al. *Neurobiology of Aging* 2006
Distribution of Alcoholism’s Effects on FA of White Matter in Men

Pfefferbaum, Adalsteinsson & Sullivan
Biological Psychiatry 2006
Distribution of Alcoholism’s Effects on FA of White Matter in Women
Redundant Targets Effect
Callosal Integrity and Alcoholism

Single Stimuli  Paired Stimuli

S1: left  S2: right  S1S2: left + right bilateral

RTE equiluminance

amplitude

Response bins

Enhanced Reaction Time

Schulte, Pfefferbaum, Sullivan *Neuropsychologia* 2004
Schulte et al. *Cerebral Cortex* 2005
Schulte et al. *NeuroImage* 2006
Selective Relationships
Callosal Regions and Cognition in Alcoholics

- Working memory
  BACKWARD DIGIT SPAN
  Hear: 3-7-2-8-1
  Say: 1-8-2-7-3
  BACKWARD BLOCK SPAN

- Visuospatial ability
  MATRIX REASONING

- Poor working memory relates to high

- Poor matrix reasoning relates to high splenium but not genu diffusivity
Regional White Matter Fiber Bundles
Alcoholism Pattern of Disruption

- Frontal and superior fibers are especially vulnerable
- Posterior and inferior fibers are relatively preserved

- FA and $\lambda$T affected in alcoholic men
- $\lambda$T affected in alcoholic women

Pfefferbaum et al. Biological Psychiatry 2009
SRI/Stanford Neuroscience Imaging Program

SRI Neuroscience Program Director
Adolf Pfefferbaum

Stanford Alcohol Neuroimaging Program Director
Edith V. Sullivan

Imaging Neuroscientists
Dirk Mayer
Natalie Zahr
Tilman Schulte
Eva Müller-Oehring
Elfar Adalsteinsson
Sandra Chanraud
Anne-Lise Pitel
Young Chul (Eugene) Jung
Meng Gu
Sonali Josan

Clinical Research Team
Margaret Rosenbloom
Rosemary Fama
Stephanie Sassoon
Priya Asok
Crystal Caldwell
Laura Horst
Karen Jackson

Animal Model Team
Natalie Zahr
Will Hawkes
Shara Vinco
Juan Orduña

Research Assistants
Will Hawkes
Shara Vinco

Image Analysis Team
Torsten Rohlfing
Mahnaz Maddah
Thomas Brosnan

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