Mixed effect model in MATLAB and its application to PD PET study

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Catherine Gallagher

W. Douglas Brown
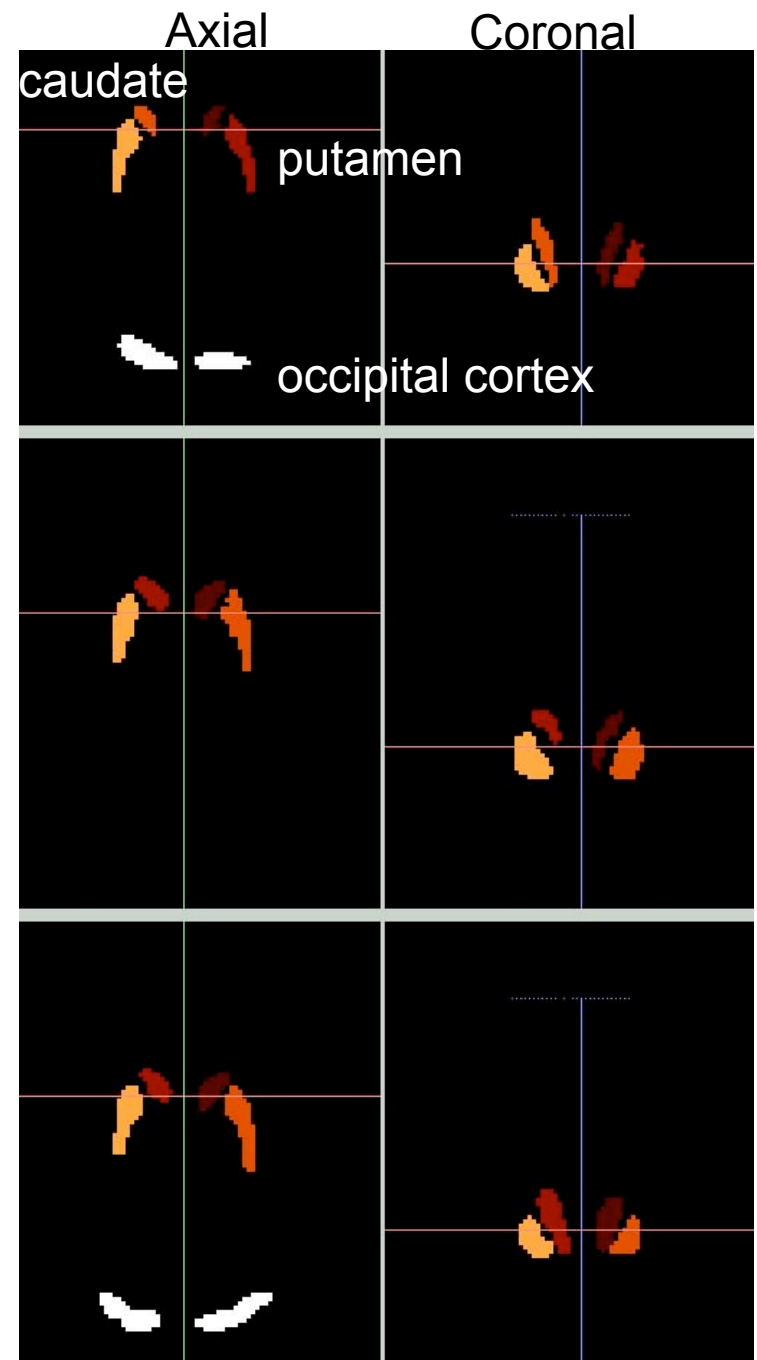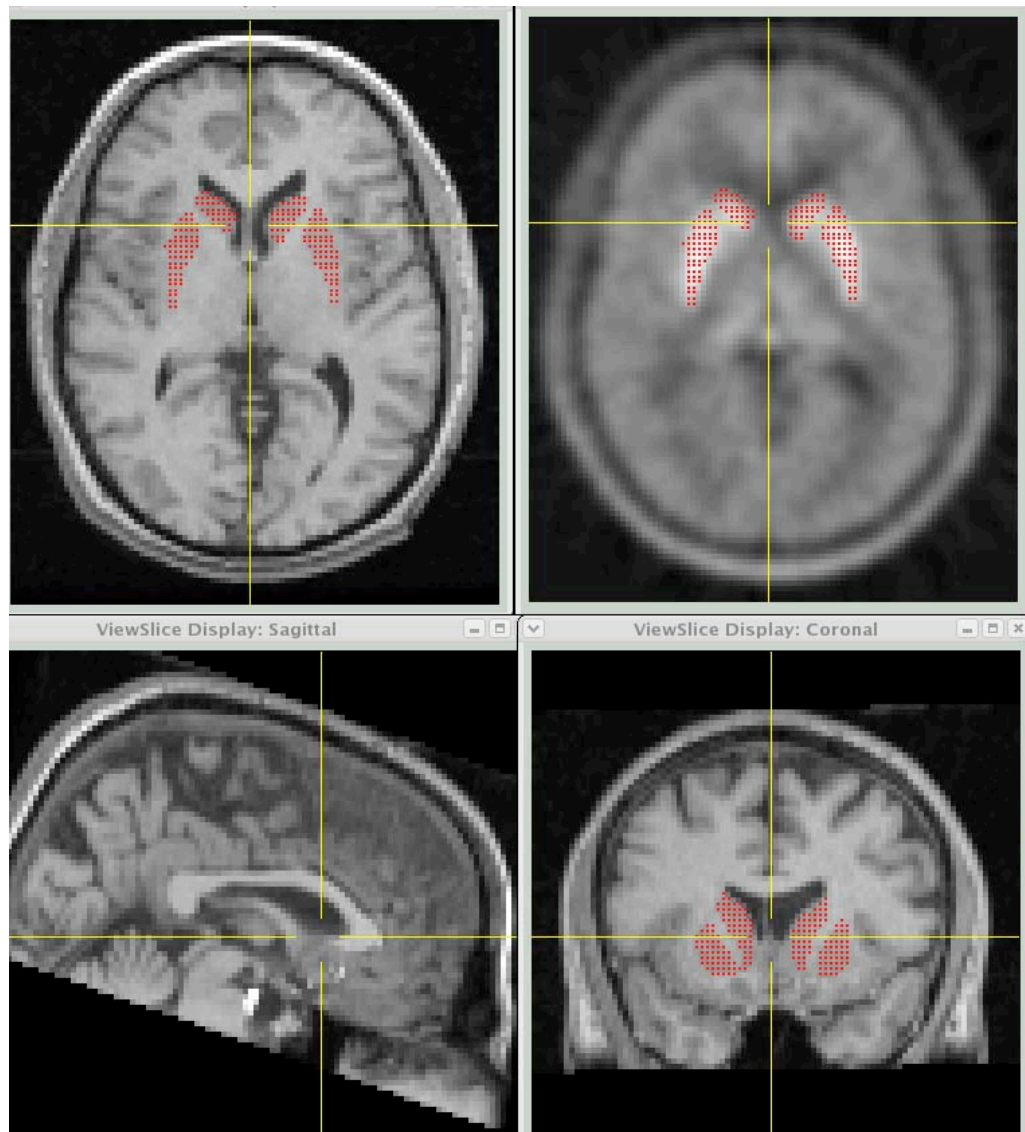
Collaborators:

Keith J. Worsley, Terry Oakes, Guofan Xu, Barbara Bendlin, Brad Christian, Sterling Johnson

Collaboration with Catherine Gallagher of the Department of Neurology

- **Parkinson's disease (PD) vs. control**
- **3 PET scans per subject– separated by 2 years**
- The study was designed and data collected by W. Douglas Brown
- PET quantiation: Using Spamalize, regions of interest were drawn over spatially normalized subject MRI scans in register with **18 dynamic fluorodopa frames**; the Patlak tool was then used to calculate **average regional uptake (K_{occ}) using an occipital cortex input function.**
- Region designations:
    - **S_putamen= symptomatic putamen (opposite the initially affected limbs)**
    - **A_putamen= asymptomatic putamen (opposite initially unaffected limbs**
    - **S_caudate= symptomatic caudate nucleus (head, body); A_caudate= asymptomatic caudate.**

Selection of regions in Spamalize

ViewSlice Display: Sagittal

ViewSlice Display: Coronal

Axial   Coronal

caudate

putamen

occipital cortex

Derivation of quantitative tracer uptake values
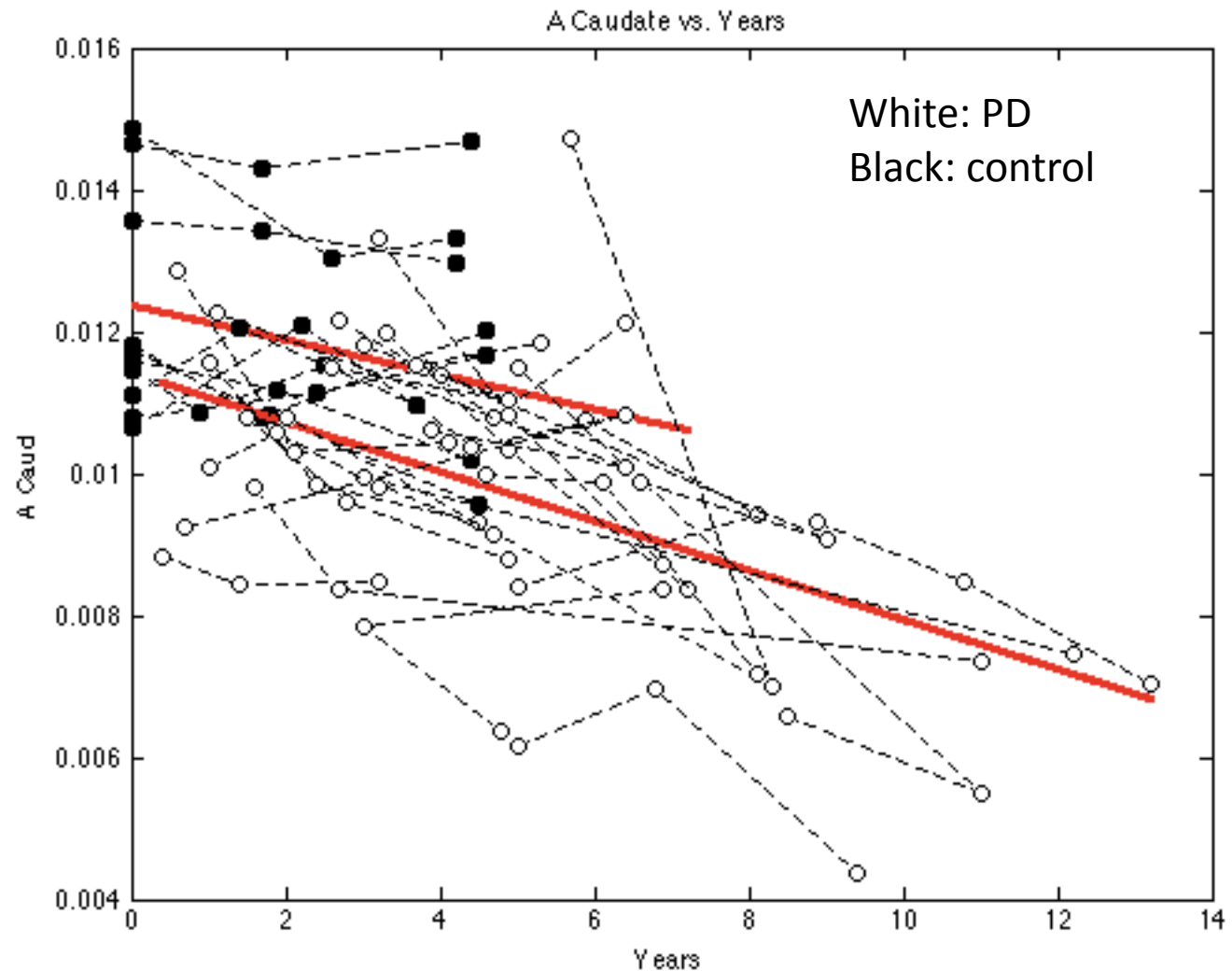
- ***18F-fluorodopa (FD) uptake rate constants – Kocc value is correlated with fluorodopa uptake and dopamine synthesis, which declines in Parkinson disease.***

- Purpose of the analysis: To quantify/model differences in radiotracer uptake over time in the striatum between Parkinson disease and control subjects.

When we use random effect models ?

- Multiple scans per subjects – longitudinal studies

- Repeated measures per subjects

Within subject variability = Between subject variability
→ Fixed effect model

Within subject variability ≠ Between subject variability
→Random effect model

A Caudate vs. Years

White: PD
Black: control

$A\_Caudate = \text{Time} + \underline{\text{Group}} + \text{Random(Subject)} + \text{error}$

putting additional error term
identical across different scans

Fixed-effect pvalue < 0.00000002
Mixed-effect pvalue = 0.0162   More conservative result !

MATLAB example - Fixed effect

> M1 = 1 + Time + Group + Subject;

> slm1 = SurfStatLinMod(s_caud, M1);

> slm1 = SurfStatT(slm1, group);

> p=pvalue(slm1.t,slm1.df)

MATLAB example - Random effect

> M1 = 1 + Time + Group + random(Subject)+I

> slm1 = SurfStatLinMod(s_caud, M1);

> slm1 = SurfStatT(slm1, group);

> p=pvalue(slm1.t,slm1.df)

A Caudate vs. Years

White: PD
Black: control
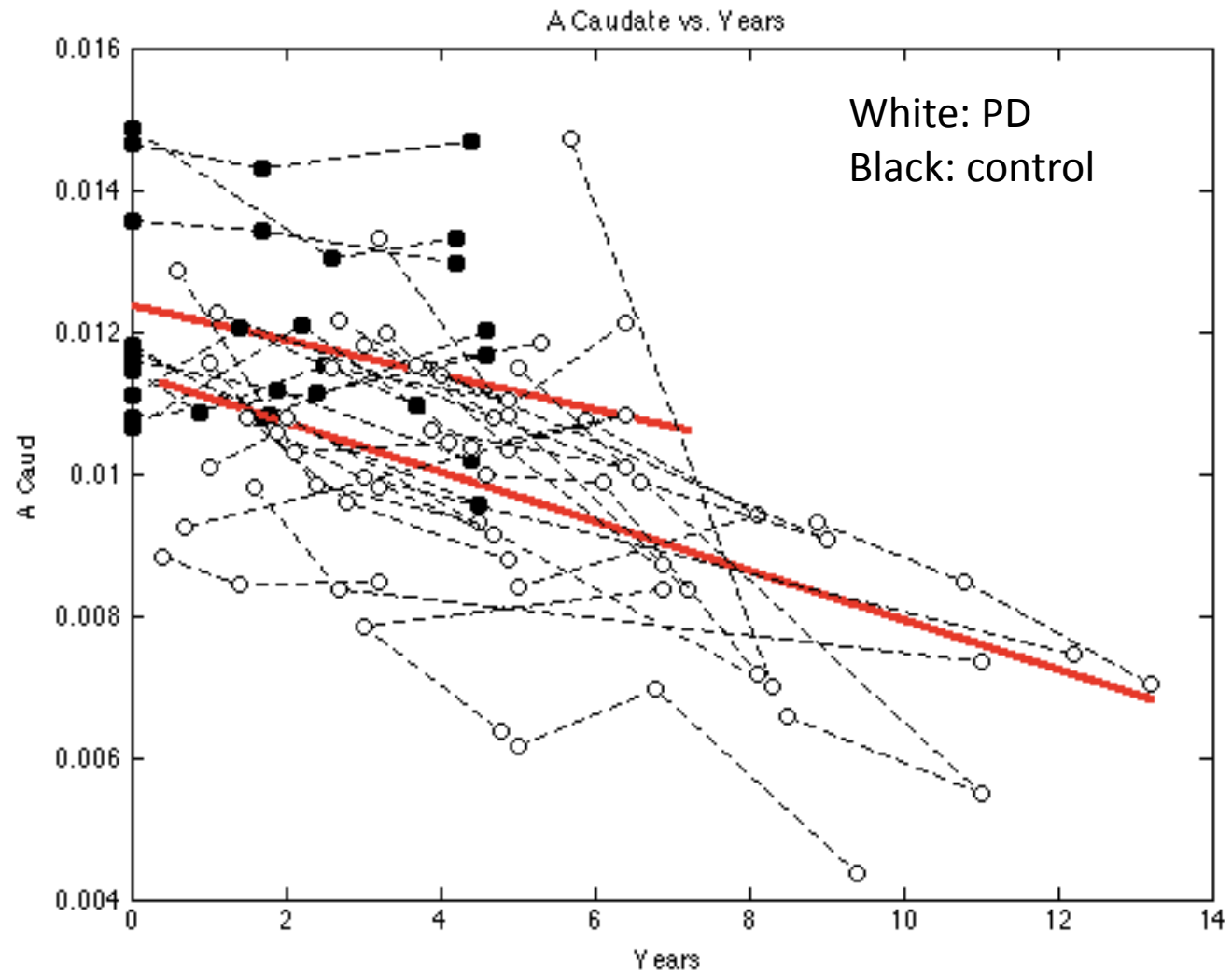
A_Caudate = Time + Group + Time*Group + random(Subject) + I

Fixed-effect pvalue = 0.008
Mixed-effect pvalue = 0.002   Better sensitivity !
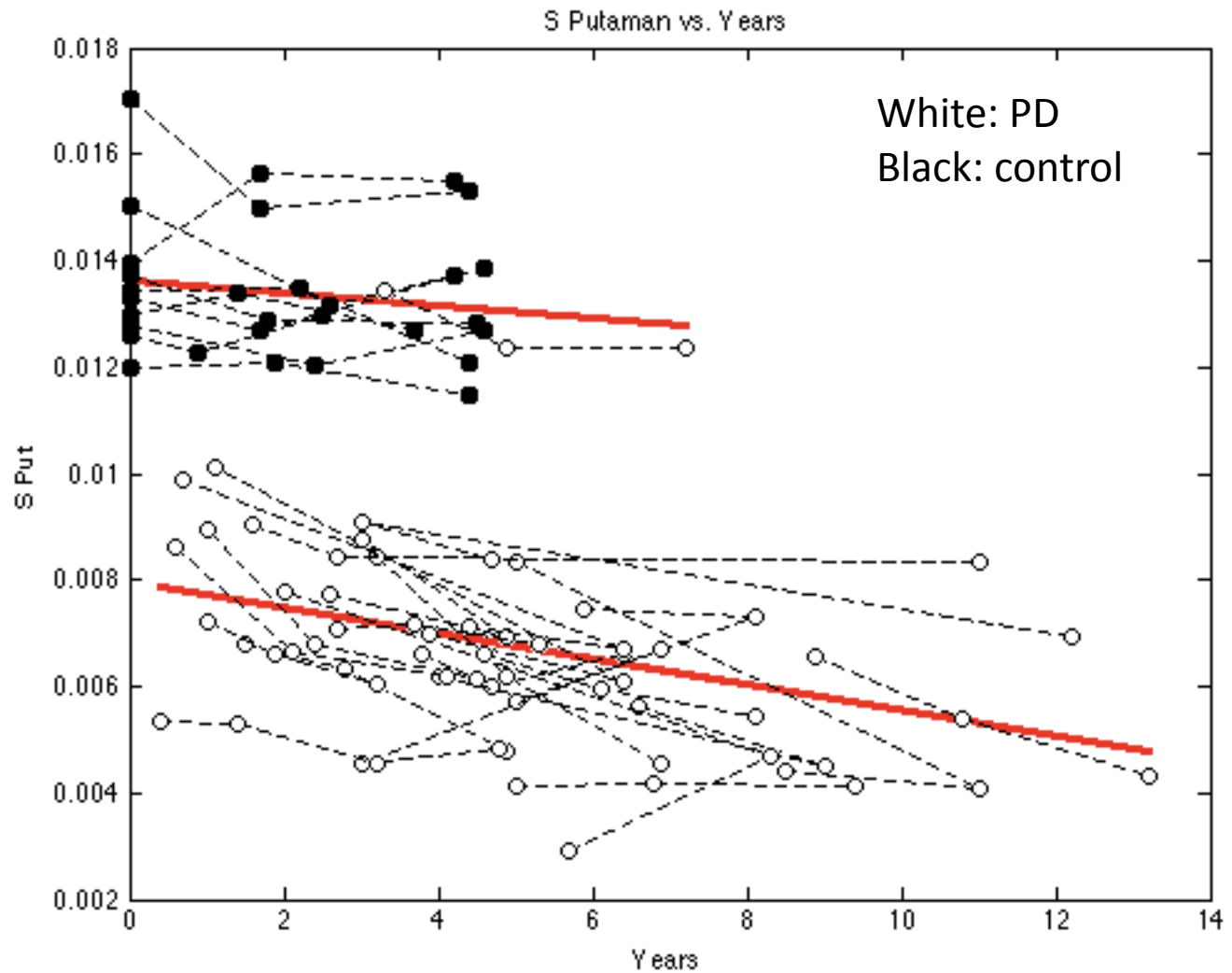
Thank you.

I am writing web pages with an easy to follow instruction with Cathy's sample data. So stay tuned. I will announce it when it is ready. Will be ready by the end of April.

S. Caudate Ki. vs. Years

White: PD
Black: control
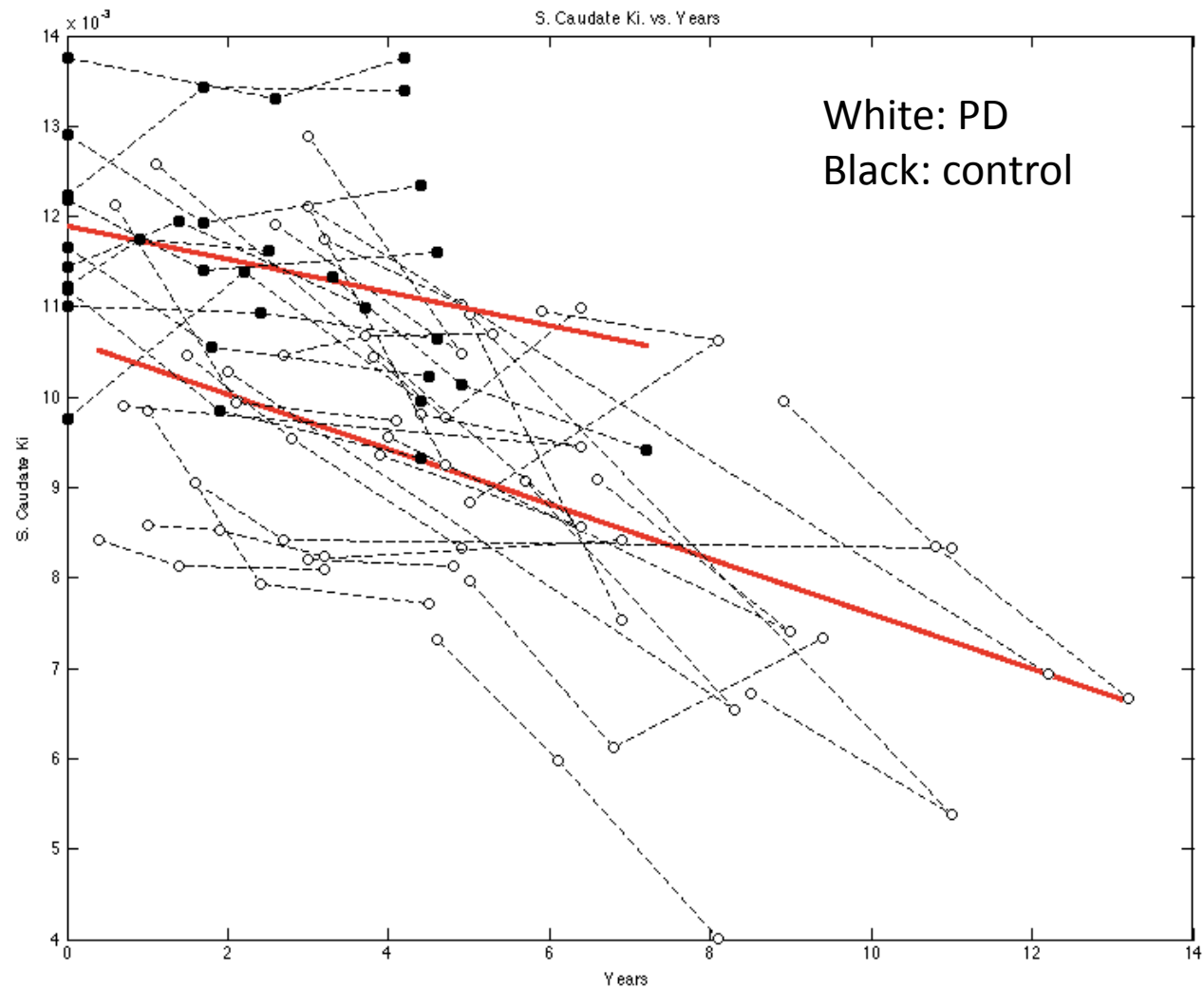
S_Caudate = Time + Group + Random(Subject) + error

Fixed-effect pvalue < 0.00000000001
Mixed-effect pvalue < 0.0022

S Putaman vs. Years

White: PD
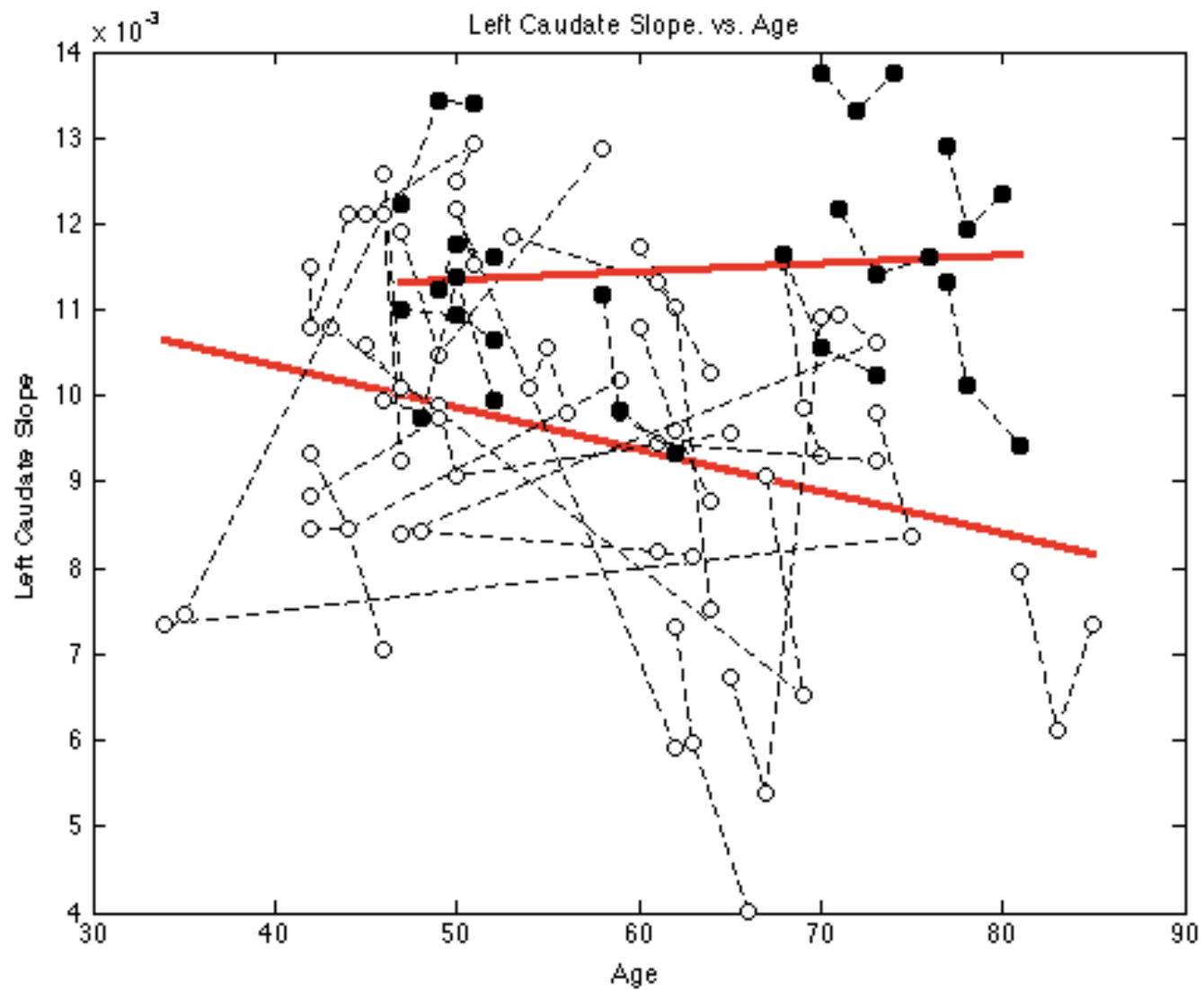Black: control

$S\_Putamen = Time + \underline{Group} + Random(Subject) + Noise$

Mixed-effect pvalue < 0.000000001

A Putaman vs. Years

White: PD
Black: control
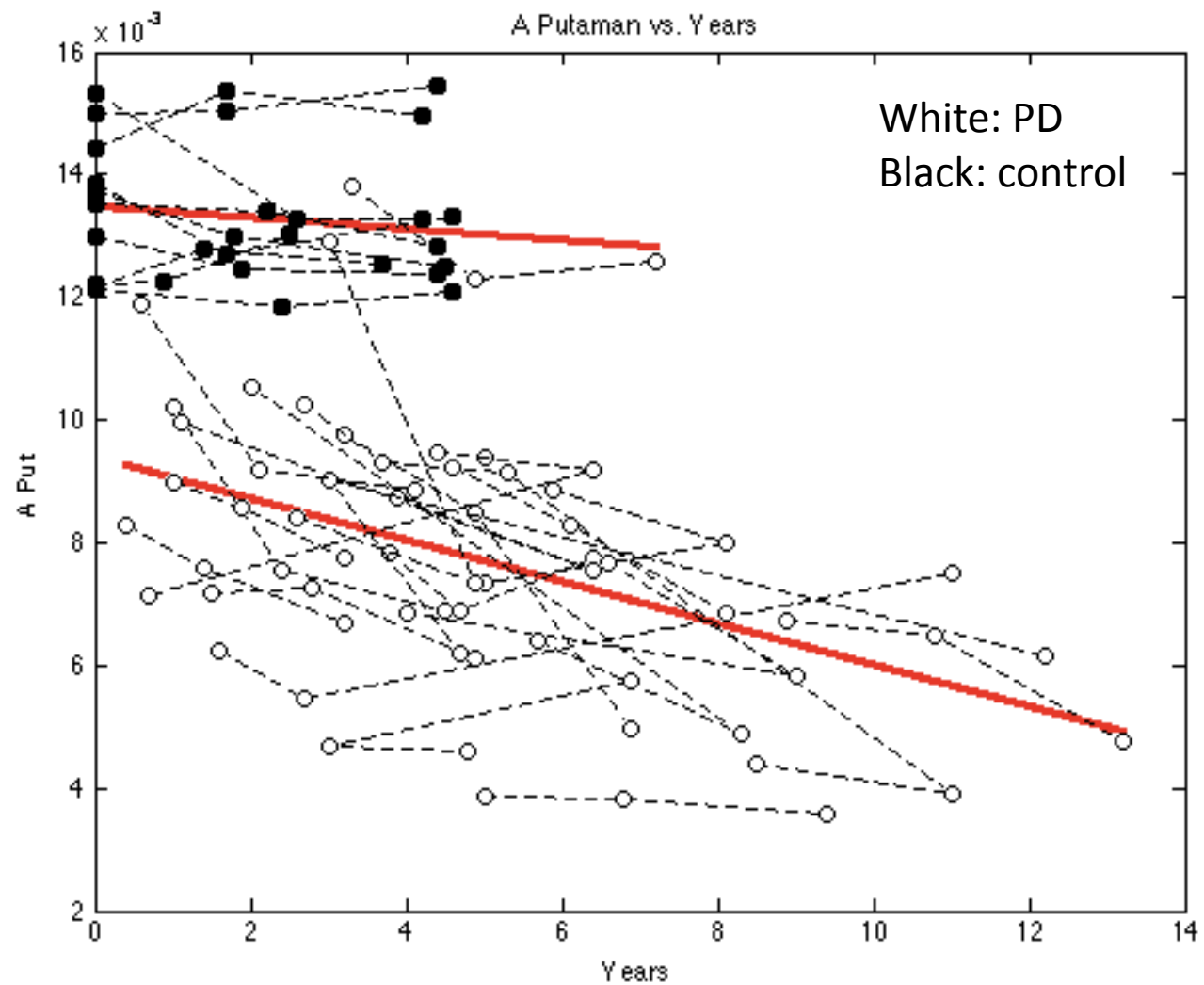
A_Putamen = Time + Group + Random(Subject) + Noise

Mixed-effect pvalue < 0.000000001

Left Caudate Slope = Age + Subject + Group