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

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• 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

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
\[ A_{\text{Caudate}} = \text{Time} + \text{Group} + \text{Random(Subject)} + \text{error} \]

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} = \text{Time} + \text{Group} + \text{Time*Group} + \text{random(Subject)} + 1

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 = Time + Group + Random(Subject) + error

Fixed-effect pvalue < 0.0000000001
Mixed-effect pvalue < 0.0022
S_Putamen = Time + Group + Random(Subject) + Noise

Mixed-effect pvalue < 0.000000001
A_Putamen = Time + Group + Random(Subject) + Noise

Mixed-effect pvalue < 0.000000001
Left Caudate Slope = Age + Subject + Group