

More than just the mean :  
Modeling intra-individual variability  
with the mixed-effects location scale model

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## **A fruitful convergence**

From a methodological point of view : “Variances are not always nuisance parameters”

Understanding the structure of variability and estimating its different components is as central as understanding the mean structure.

From a psychological point of view : short-term intra-individual variability can be a conceptual tool

We, as psychologists, use quantifications and models of intra-individual variability to measure and describe human functional and dynamic characteristics.

This reinforces the need to a deeper investigation on intra-individual variability above and beyond the normative view of mean values and heterogeneity among subjects.

# Plan

1. Quantifying intra-individual variability
2. Modeling between-subject and within-subject variances using mixed-effects location scale models
3. A Bayesian model for estimating intra-individual variability as a predictor

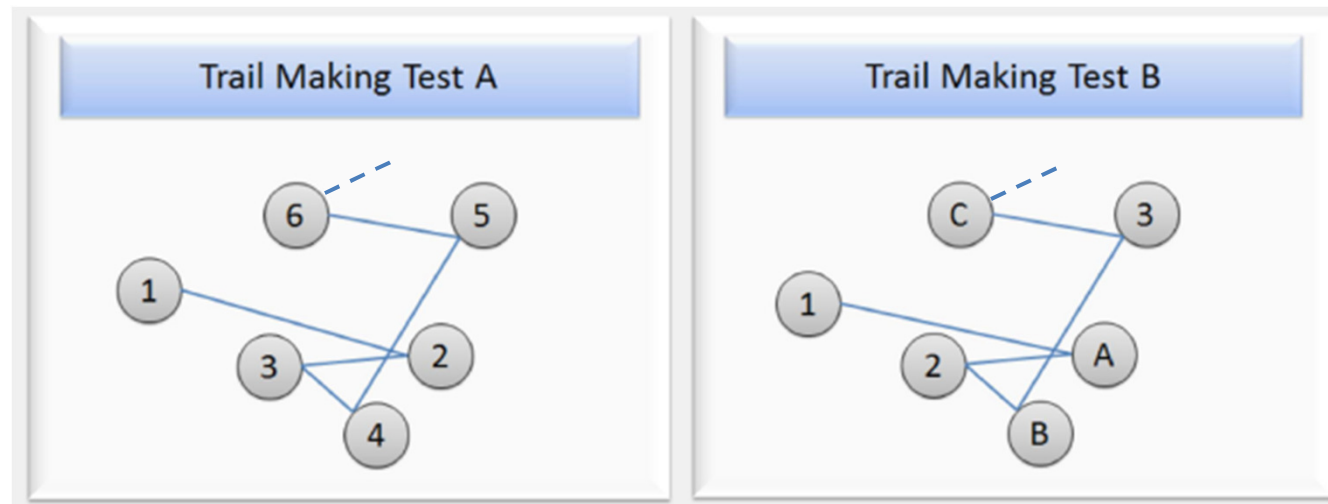
# The analyzed data

Participants and procedure :

Thirty-five adults aged 61-97 years (mean age 71 years), MMSE > 25. Eight measurement occasions, every two weeks (data collected by J. Lebahar, Phd).

At each measurement occasion :

*Trail Making Test*

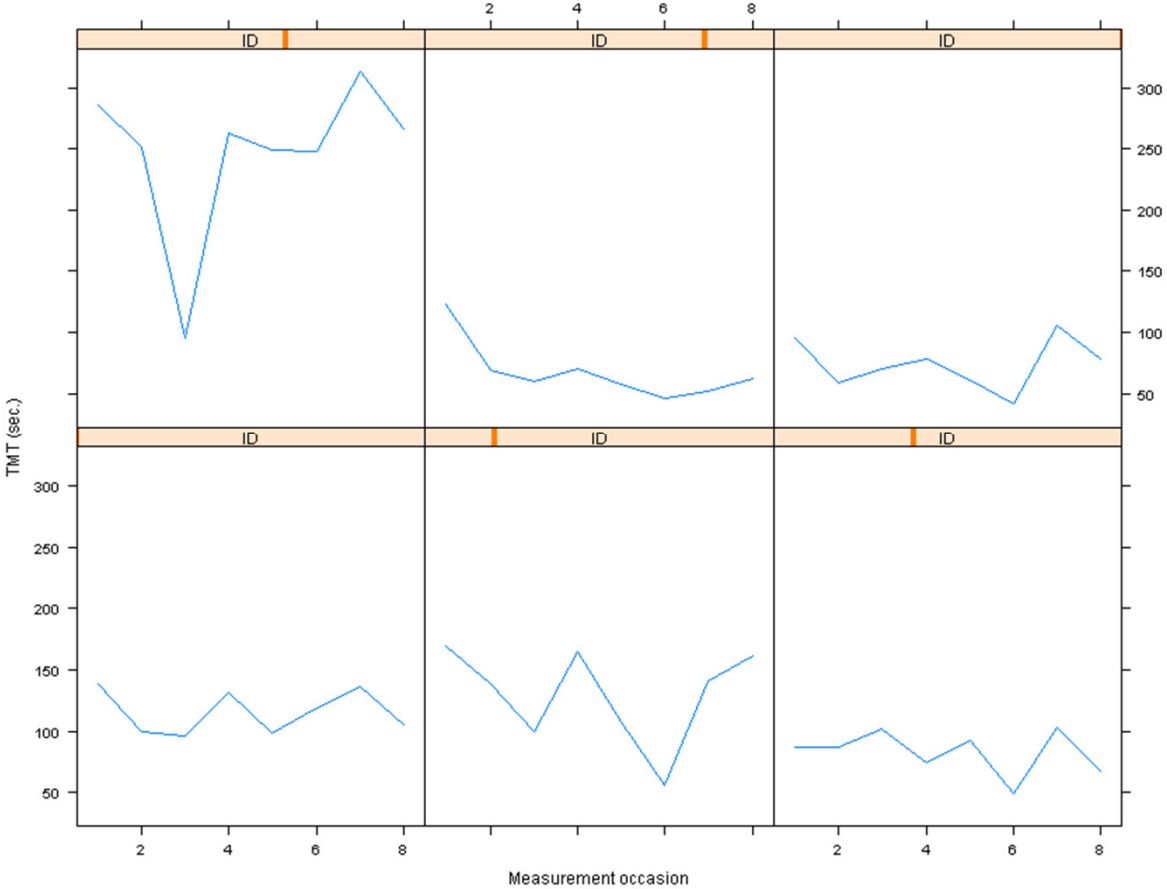


Realization time in sec.

# The analyzed data

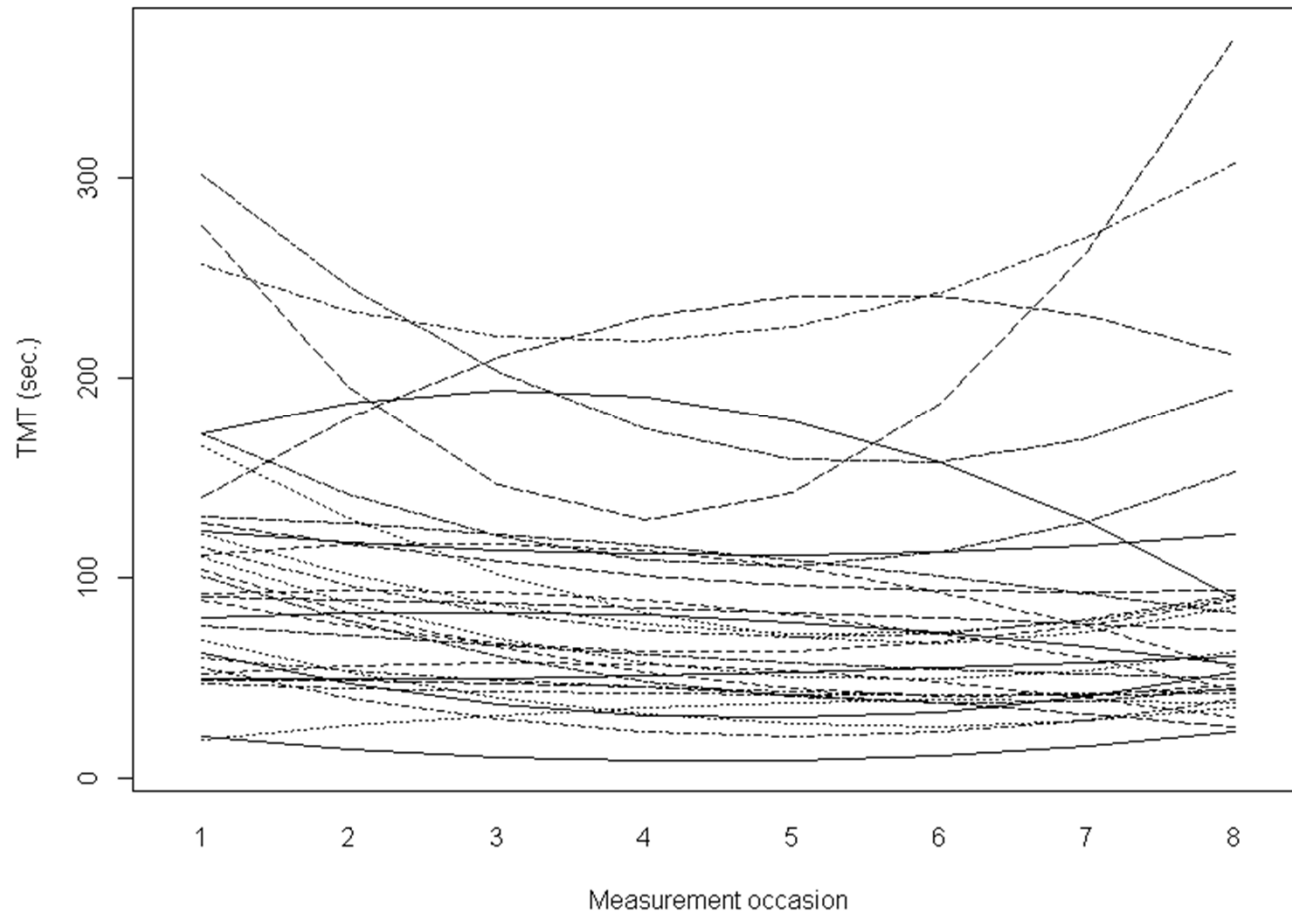
## *Intra-individual variability of Realization Time for the Trail Making Test*

The first 6 participants



# The analyzed data

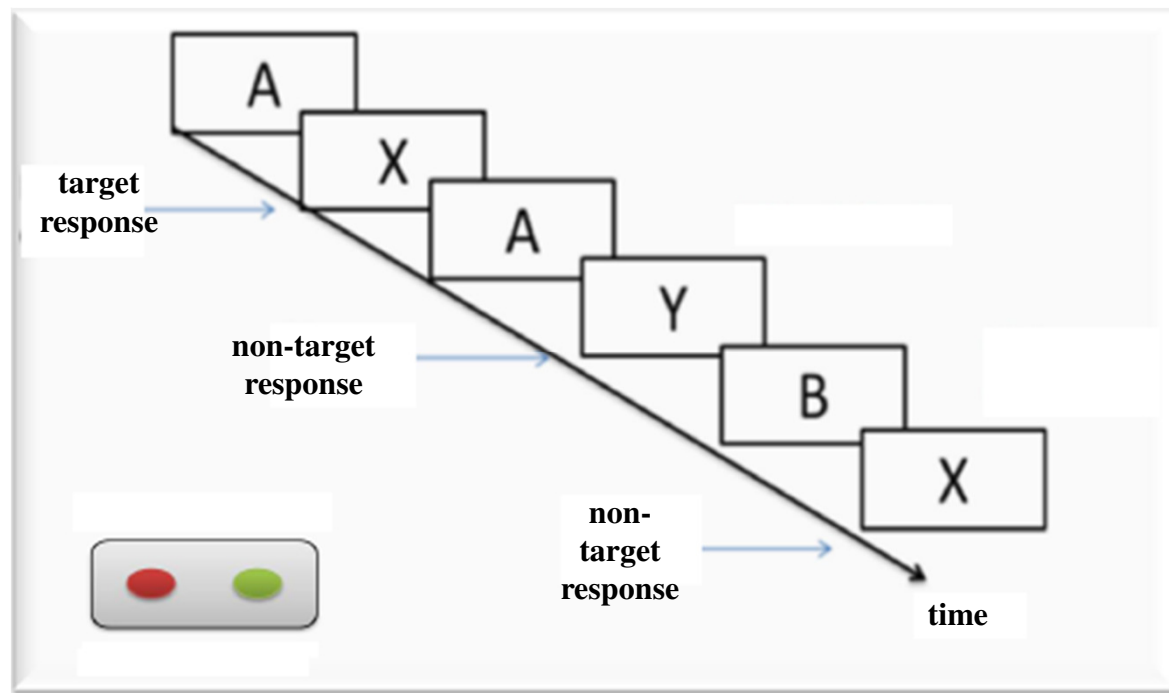
*IDs in IIV in Realization Time for the Trail Making Test*



# The analyzed data

At each measurement occasion :

*The AX-Continuous Performance Test* : 100 trials (40 AX, 20 AY, 20 BX, 20 BY) : RT for correct responses.

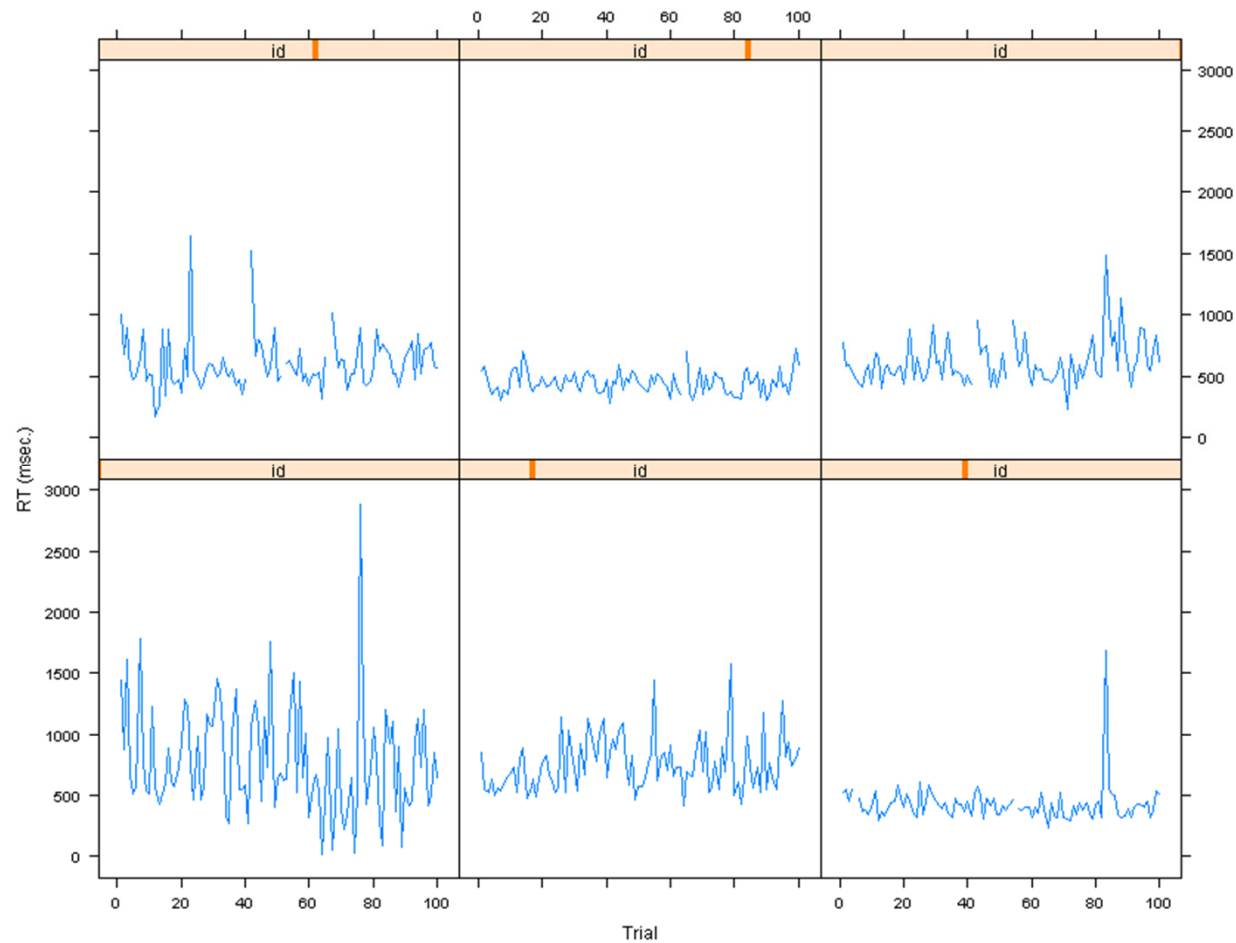


Reaction time (RT) in sec.

# Data from an illustrative example

*Intra-individual variability of Reaction Time for AX-CPT (session 3)*

The first 6 participants





Quantifying intra-individual variability

## A two-stage approach

### *Stage 1*

Estimation of one or another index of IIV on the basis of observations at the individual level.

→ Each estimate has its own error of estimation.

### *Stage 2*

IIV as an outcome :

- regression of IIV on one or several covariates of interest.

IIV as a predictor :

- regression of one or several outcomes of interest on IIV.

→ More often, the SE of estimation will be downwardly biased and the probability of rejecting a null hypothesis although it is true (Type I error) will be inflated.

## Some conventional methods for quantifying intra-individual variability

*The amplitude of intra-individual variability (ISD)*

$Y_{t,i}$  : the observed score of individual  $i$  at occasion  $t$  ;

$T_i$  : the number of measurement occasions for individual  $i$  ;

$$\text{raw-score } ISD_i = \sqrt{\frac{\sum (y_{t,i} - y_i.)^2}{T_i - 1}} \text{ and raw-score } ISD_i^2.$$

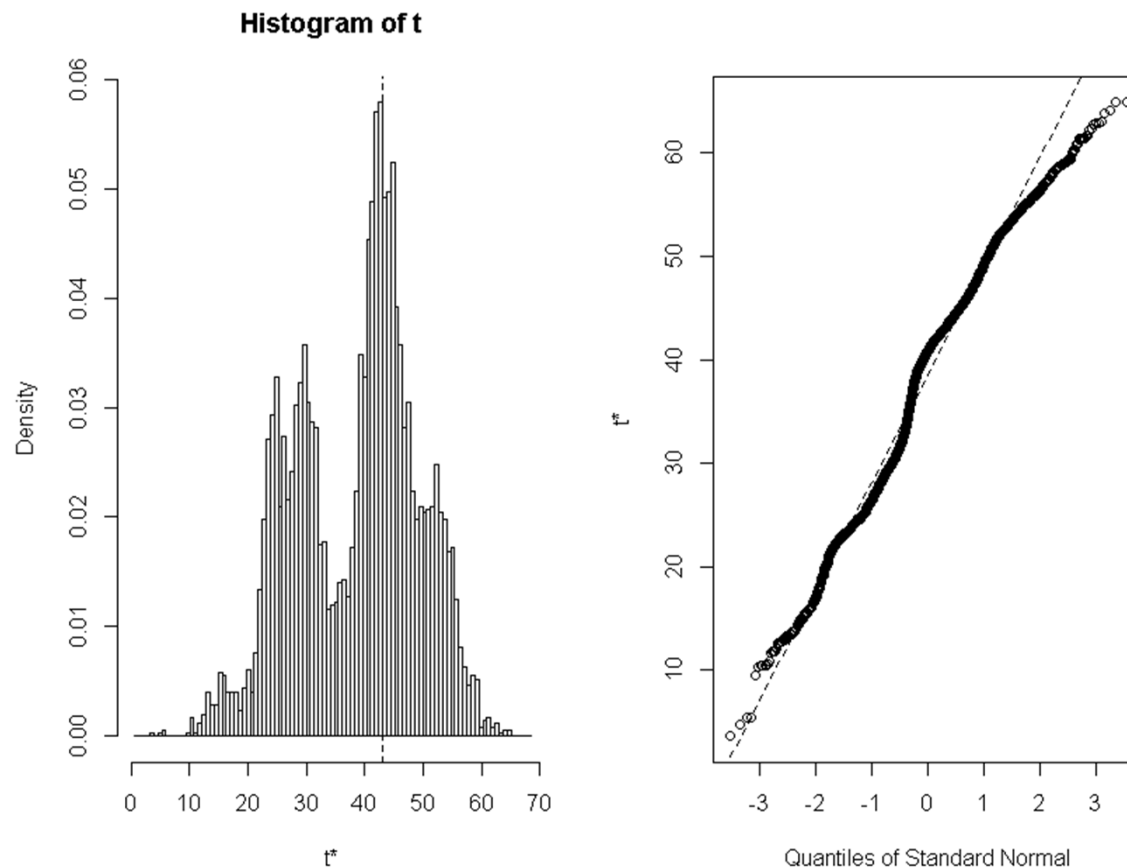
No consideration of temporal order or serial correlation.

*Practical*

→ An application with R

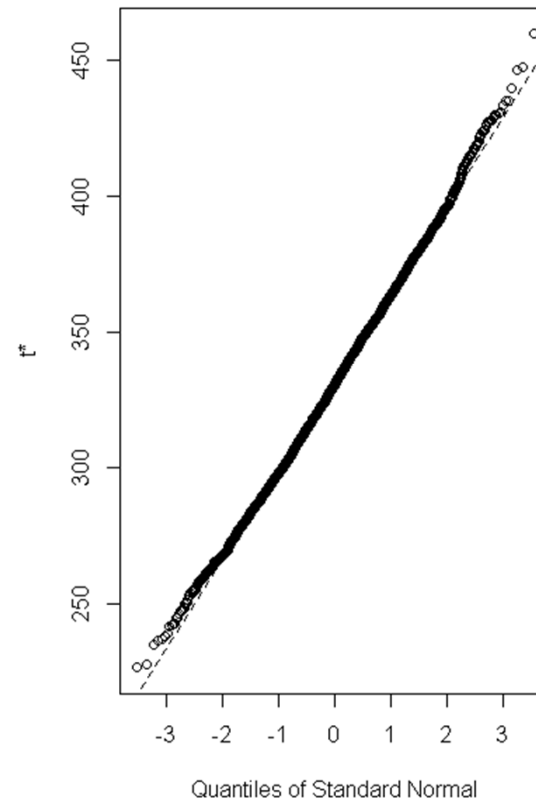
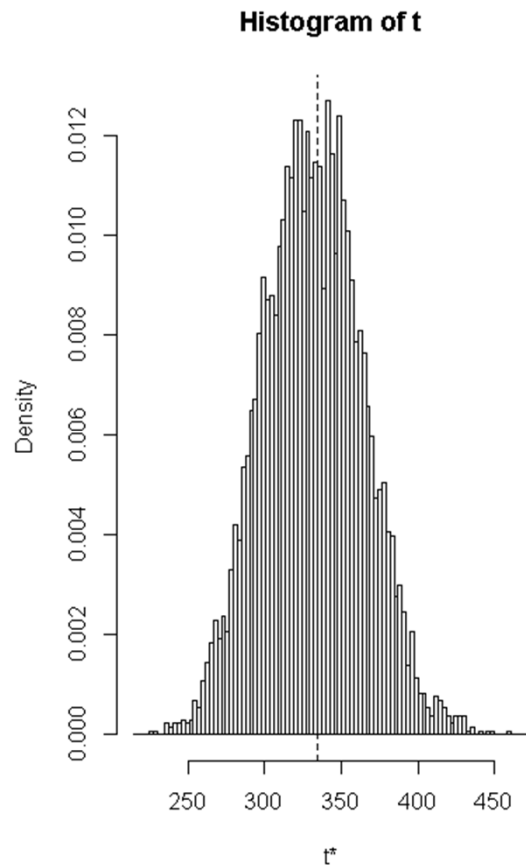
# Some conventional methods for quantifying intra-individual variability

TMTb : empirical distribution of *ISD* for subject 2 (5000 bootstrap samples);  $ISD = 43.04$ , 95% IC [17.63, 56.19].



# Some conventional methods for quantifying intra-individual variability

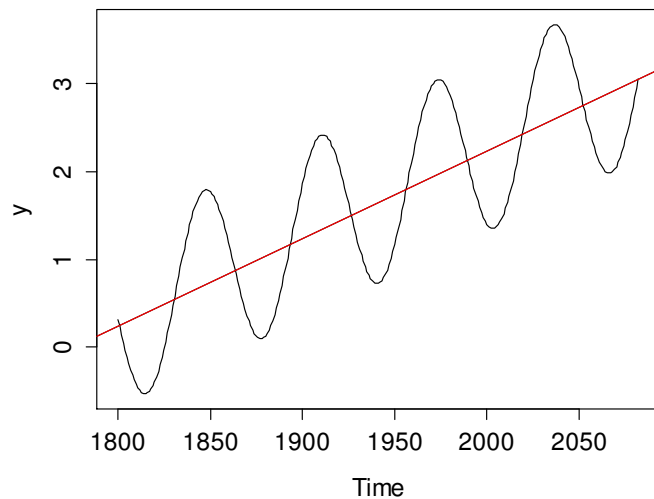
AX-CPT Reaction Time : empirical distribution of  $ISD$  for subject 1 (5000 bootstrap samples);  $ISD = 334$ , 95% IC [269, 396].



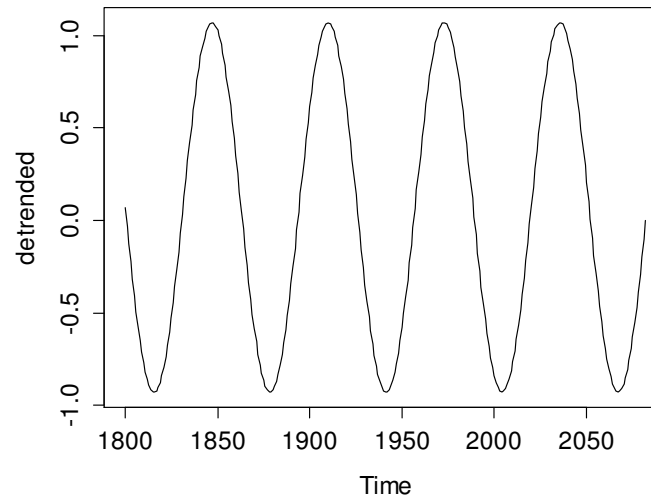
# Some conventional methods for quantifying intra-individual variability

$ISD$  and  $ISD^2$  are sensitive to systematic intra-individual change (trends).

→ detrending the data :



$$ISD_y = 1.079$$



$$\text{detrended } ISD_y = 0.704$$

Raw-score  $ISD$  and  $ISD^2$  are likely to be correlated with individual mean scores.

Raw-score Individual Coefficient of Variation ( $ICV$ ) and detrended  $ICV$ .

# Some conventional methods for quantifying intra-individual variability

*The temporal dependency in the data*

The autocorrelation or the degree to which current observations are correlated with previous observations.

The autocorrelations can be obtained for different lags.

$\rho_i(\tau)$  is the autocorrelation at lag  $\tau$  ( $\tau = 1, 2, \dots$ ) with :

$$\hat{\rho}_i(\tau) = \frac{\hat{\gamma}_i(\tau)}{ISD_i^2}$$

$\hat{\gamma}_i(\tau)$  is the auto-covariance at lag  $\tau$  defined by the covariance between pairs of observations that are formed by  $y_{t,i}$  and  $y_{t+\tau,i}$ .

*Practical*

→ An application with R

## Some conventional methods for quantifying intra-individual variability

### *The degree of temporal instability*

Refers to occasion-to-occasion squared differences and combines both the amplitude of intra-individual variability and the temporal dependency.

The mean square successive difference (*MSSD*) :

$$MSSD_i = \frac{1}{T_i - 1} \sum_{t=1}^{T-1} (y_{t+1,i} - y_{t,i})^2$$

Given stationary data,  $MSSD_i = 2ISD_i^2(1 - \hat{\rho}_i(1))$ .

The MSSD is a lag-dependent measure.

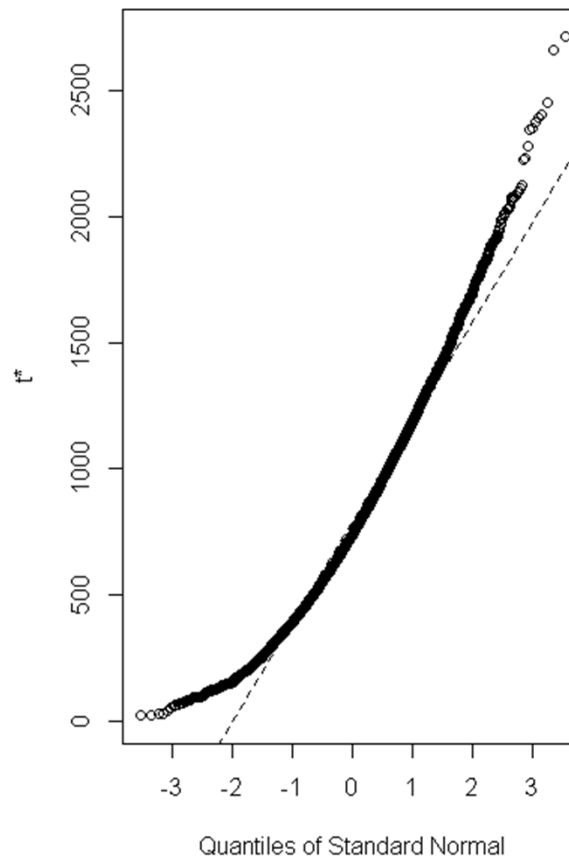
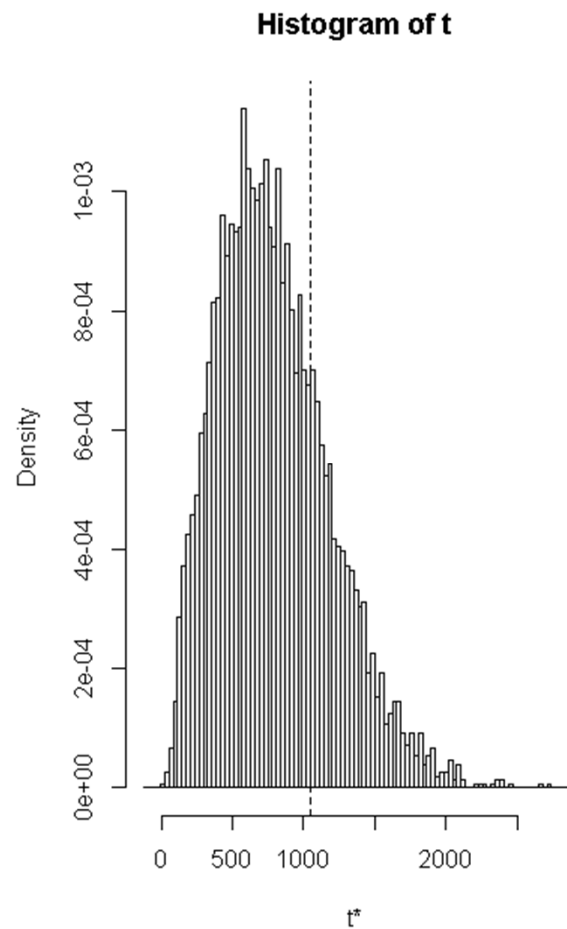
### *Practical*

→ An application with R



# Some conventional methods for quantifying intra-individual variability

TMTb : empirical distribution of mssd for subject 1 (5000 bootstrap samples); mssd = 1050, 95% IC [166, 1683].



Modeling between-subject and  
within-subject variances using  
mixed-effects location scale models

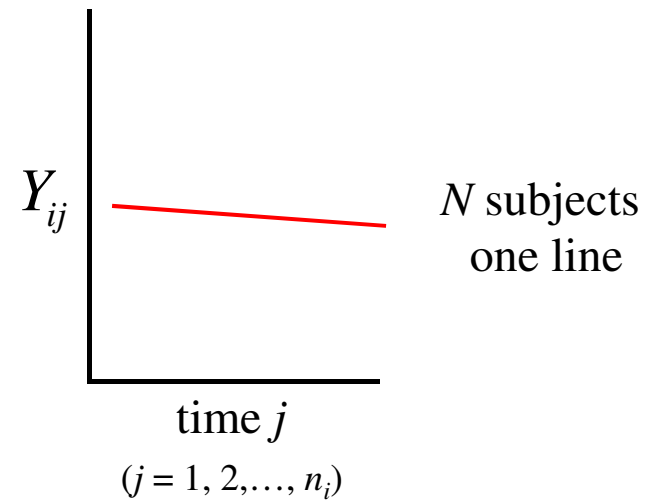
# Simple linear regression on time

Measurement  $y$  of subject  $i$  ( $i = 1, 2, \dots, N$ ) on occasion  $j$  ( $j = 1, 2, \dots, n_i$ )

$$Y_{ij} = \underbrace{\beta_0 + \beta_1 \times \text{time}_j}_{\text{fixed part}} + \underbrace{e_i}_{\text{random part}}$$

where

$$e_i \sim \mathcal{N}(0, \sigma^2)$$

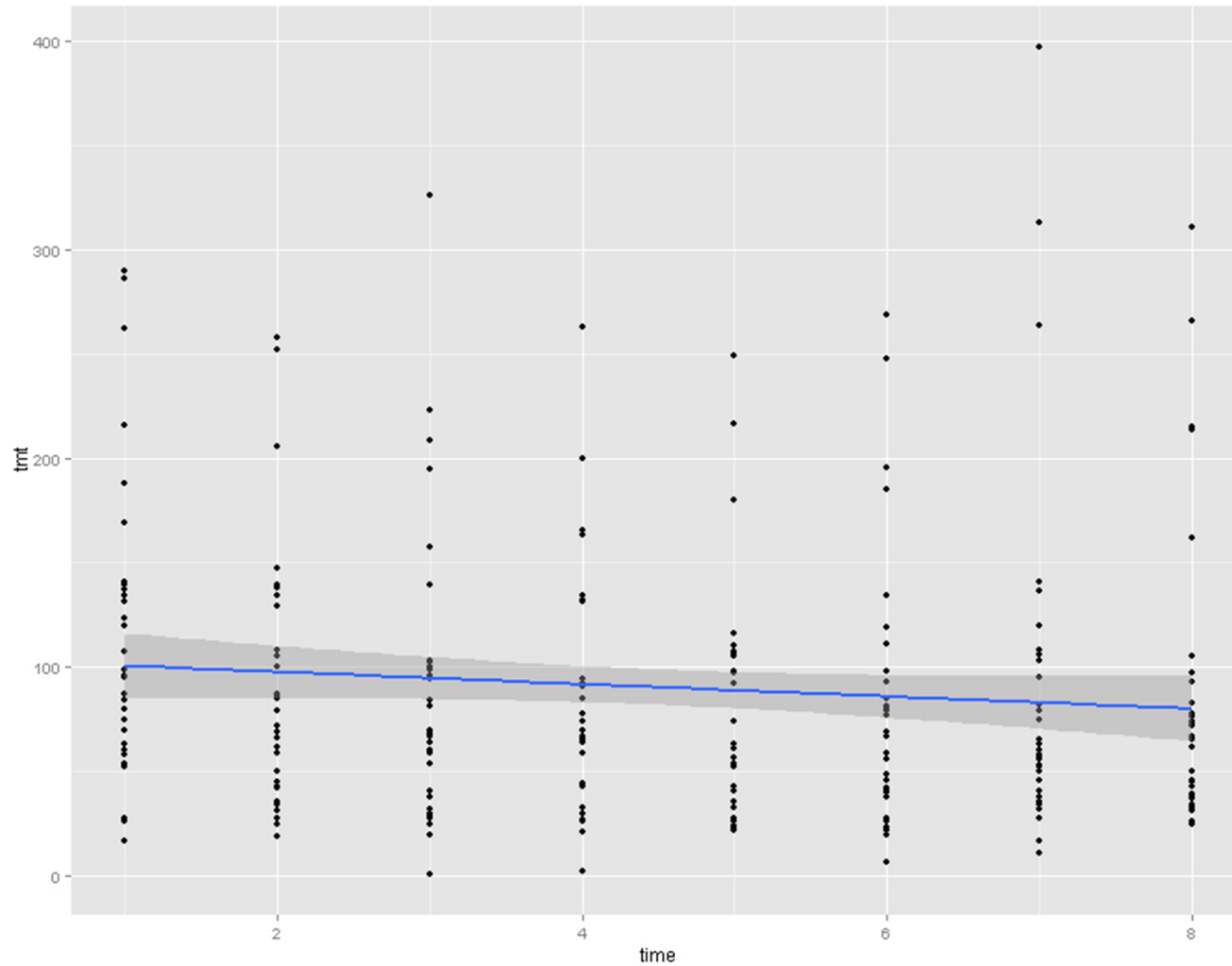


*Practical*

→ An application with R

# Simple linear regression on time

*TMT Realization Time* : Evolution of performance over time : linear trend



# The mixed-effects regression model as a primary method for analysis of repeated and longitudinal data

*MRMs account for the influence of subjects on their repeated observations*

Random subject effects reflect each subject's performance or development across time.

Random subject effects = between-subjects (BS) differences in intercept, linear slope, quadratic slope, etc. of the regression function.

Differences between subjects are measured by the variance of the random effects :

- the BS (inter-individual) variance,
- the within-subjects (WS) or intra-individual variance.

# The mixed-effects regression model as a primary method for analysis of repeated and longitudinal data

*The two-level random intercept model*

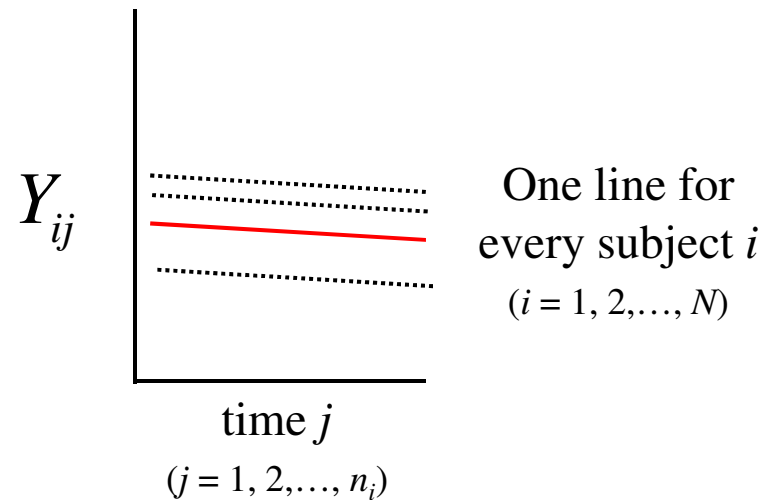
Measurement  $y$  of subject  $i$  ( $i = 1, 2, \dots, N$ ) on occasion  $j$  ( $j = 1, 2, \dots, n_i$ )

$$Y_{ij} = \underbrace{\beta_0 + \beta_1 \times \text{time}_j}_{\text{fixed part}} + \underbrace{v_i + \varepsilon_{ij}}_{\text{random part}},$$

where

$$v_i \sim \mathcal{N}(0, \sigma_v^2) \rightarrow \text{BS variance}$$

$$\varepsilon_{ij} \sim \mathcal{N}(0, \sigma_\varepsilon^2) \rightarrow \text{WS variance}$$



# The mixed-effects regression model as a primary method for analysis of repeated and longitudinal data

*The two-level random intercept model*

Measurement  $y$  of subject  $i$  ( $i = 1, 2, \dots, N$ ) on occasion  $j$  ( $j = 1, 2, \dots, n_i$ ) :

$$y_{ij} = x'_{ij}\beta + v_i + \varepsilon_{ij} \quad (1)$$

$x_{ij}$  is the  $p \times 1$  vector of regressors ;

$\beta$  is the  $p \times 1$  vector of regression coefficients ;

$v_i$  : random effects for intercepts,

$$v_i \sim \mathcal{N}(0, \sigma_v^2), \sigma_v^2 \text{ represents the BS variance ;}$$

$\varepsilon_{ij}$  : residual “random” effects that are assumed to be independent of  $v_i$ ,

$$\varepsilon_{ij} \sim \mathcal{N}(0, \sigma_\varepsilon^2), \sigma_\varepsilon^2 \text{ represents the WS variance.}$$

$\sigma_v^2$  and  $\sigma_\varepsilon^2$  are supposed to be homogeneous across subject groups or levels of covariates.

# The mixed-effects regression model as a primary method for analysis of repeated and longitudinal data

*In the long format, each row is one time point per subject*

The stacked data set :

---

ID	time	age	fab	tmta	tmtb	tmt
1	1	68	18	60	199	139
1	2	68	18	41	141	100
1	3	68	18	56	152	96
1	4	68	18	46	178	132
1	5	68	18	42	140	98
1	6	68	18	43	162	119
1	7	68	18	49	185	136
1	8	68	18	53	158	105
2	1	88	16	37	206	169
2	2	88	16	34	173	139
2	3	88	16	39	139	100
2	4	88	16	35	200	165
2	5	88	16	37	144	107
2	6	88	16	29	85	56
2	7	88	16	39	180	141
2	8	88	16	51	213	162
...	...	...	...	...	...	...

---

*Practical*

→ An application with R



# The mixed-effects regression model as a primary method for analysis of repeated and longitudinal data

*Evolution with time and effect of age on the trail making test performance.*

Results of the Chi-square test used to compare mrm1 and mrm2 :

```
Models:
mrm1: tmt ~ time + (1 | ID)
mrm2: tmt ~ time + age + (1 | ID)
      Df    AIC    BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
mrm1  4 2589.2 2603.3 -1290.6  2581.2
mrm2  5 2581.7 2599.2 -1285.8  2571.7 9.6003      1 0.001945 **
```

Smaller is better !

The RSS reduction is statistically significant

# The mixed-effects regression models as a primary method for analysis of repeated and longitudinal data

*TMT performance : Evolution with time and effect of age*

```
Linear mixed model fit by REML ['lmerMod']
Formula: tmt ~ time + age + (1 | ID)
Data: tmt31
```

Random effects:

Groups	Name	Variance	Std.Dev.	
ID	(Intercept)	2505	50.05	→ BS variance : $\sigma_v^2$
	Residual	1336	36.55	→ WS variance : $\sigma_\epsilon^2$

Number of obs: 248, groups: ID, 31

Fixed effects:

	Estimate	Std. Error	t value	
(Intercept)	-115.6516	68.3211	-1.693	$\beta_0$ : constant term
time	-2.9228	1.0130	-2.885	$\beta_1$ : time → tmt
age	2.8758	0.8863	3.245	$\beta_2$ : age → tmt

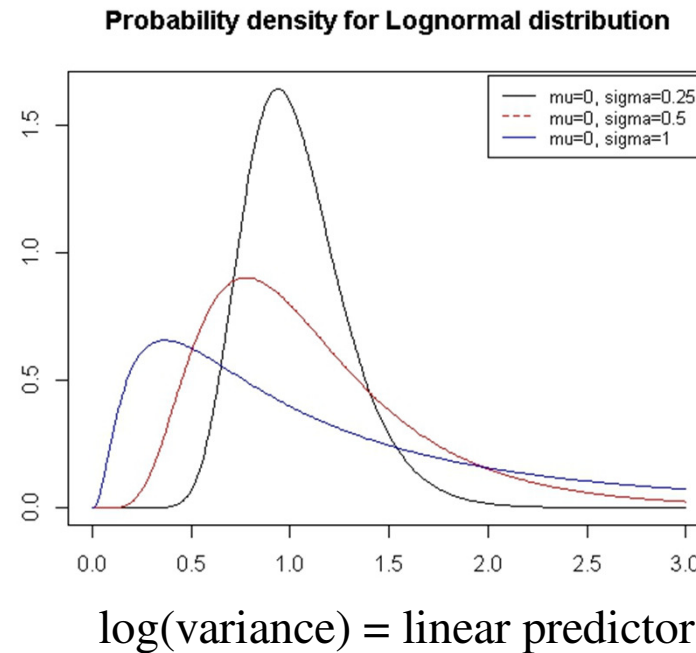
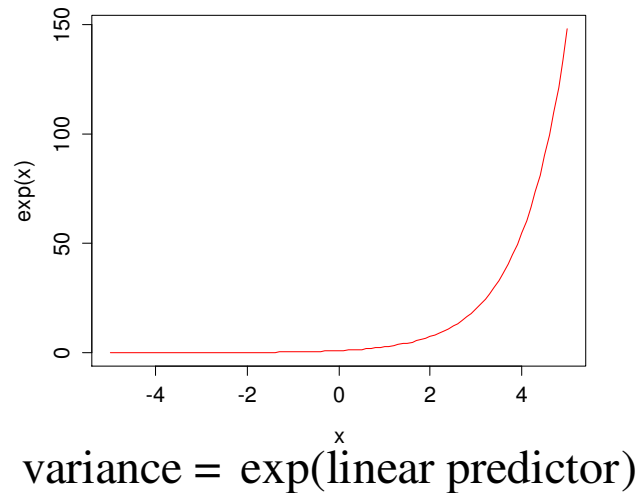
Correlation of Fixed Effects:

	(Intr)	time
time	-0.067	
age	-0.988	0.000

# The mixed-effects location scale model

Assumptions that  $\sigma_v^2$  and  $\sigma_\epsilon^2$  are homogeneous across subject groups or levels of covariates can be relaxed.

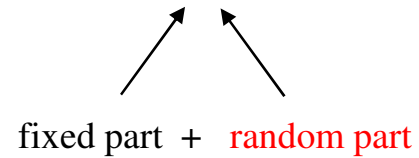
→ *Using a log-linear representation for variances (to ensure positive variances)*



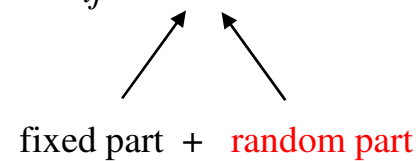
# The mixed-effects location scale model

$$y_{ij} = x'_{ij}\beta + v_i + \varepsilon_{ij} \tag{1}$$

BS variance :  $\sigma^2_{v_i} = \exp(\mathbf{u}'_i\boldsymbol{\alpha})$  or  $\log(\sigma^2_{v_i}) = \mathbf{u}'_i\boldsymbol{\alpha}$  (2)



WS variance :  $\sigma^2_{\varepsilon_{ij}} = \exp(\mathbf{w}'_{ij}\boldsymbol{\tau})$  or  $\log(\sigma^2_{\varepsilon_{ij}}) = \mathbf{w}'_{ij}\boldsymbol{\tau}$  (3)



# The mixed-effects location scale model

→ *Some covariates can influence the BS and WS variances.*

BS variance : - subject-level covariates →  $\log(\sigma_{v_i}^2)$

WS variance : - subject-varying covariates →  $\log(\sigma_{\varepsilon_{ij}}^2)$

- time-varying covariates →  $\log(\sigma_{\varepsilon_{ij}}^2)$

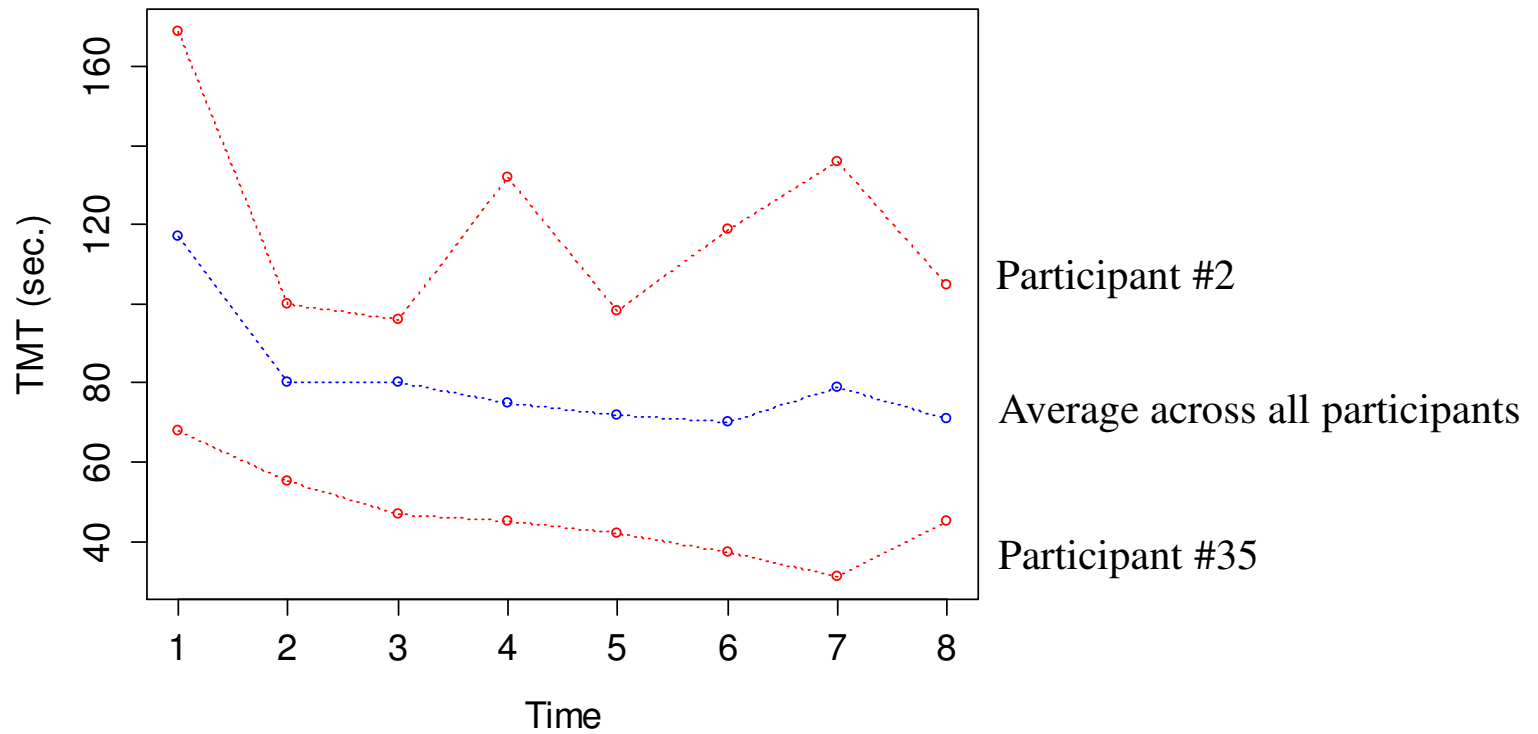
- residual variation across subjects :  $\log(\sigma_{\varepsilon_{ij}}^2) = \mathbf{w}'_{ij} \boldsymbol{\tau} + \omega_i$

$$\omega_i \sim N(0, \sigma_{\omega}^2)$$

↑  
random subject  
(scale) effects

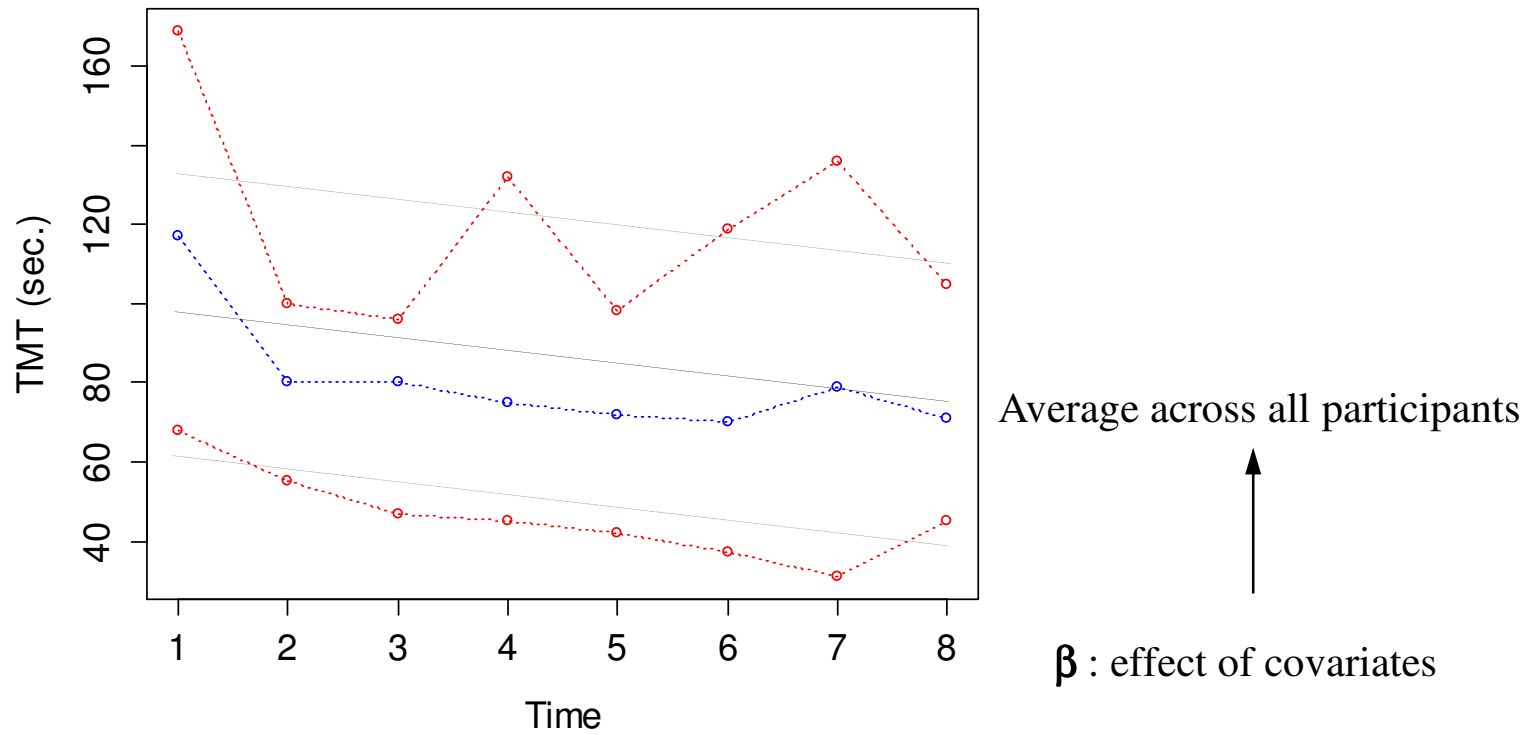
# The mixed-effects location scale model

Measurement  $y$  of subject  $i$  ( $i = 1, 2, \dots, N$ ) on occasion  $j$  ( $j = 1, 2, \dots, n_i$ )



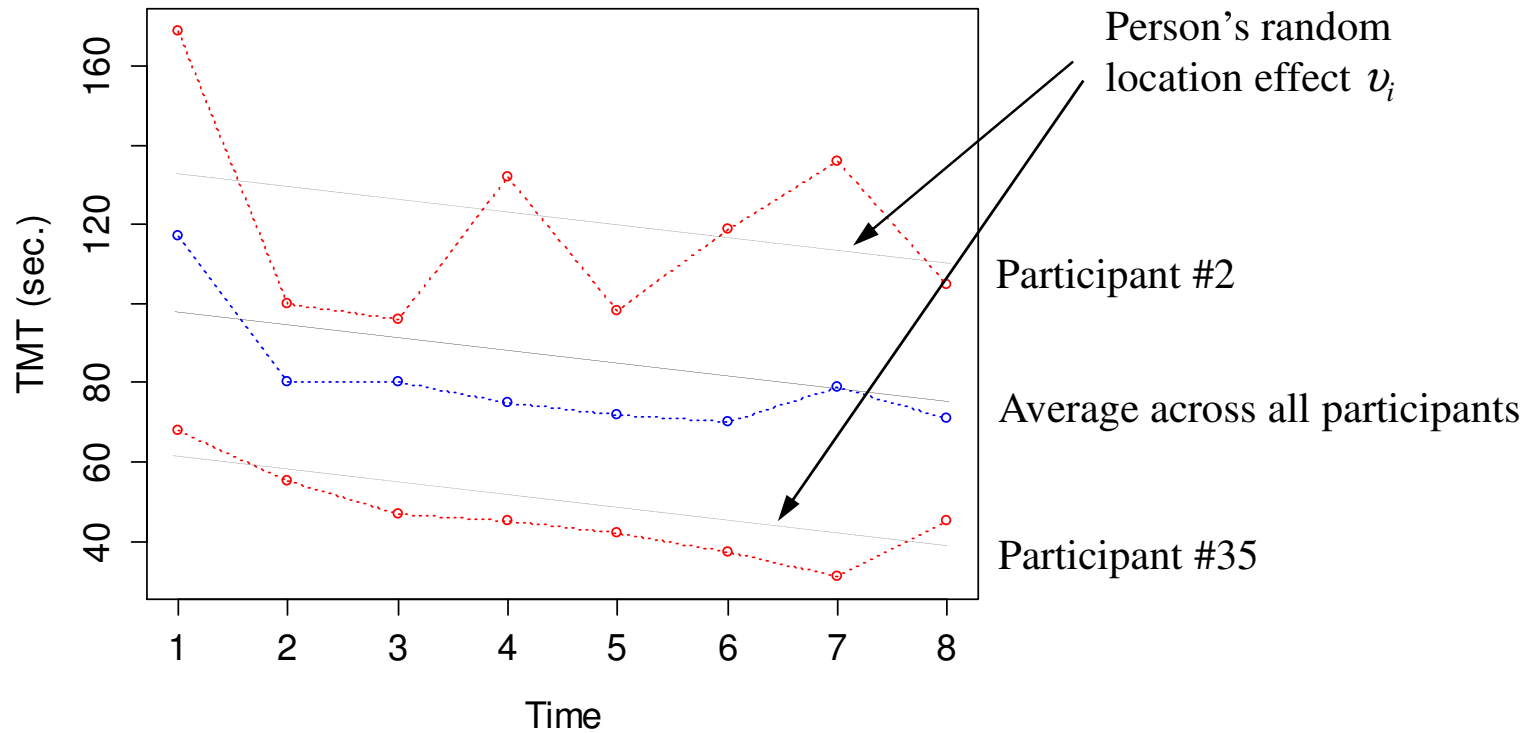
# The mixed-effects location scale model

Measurement  $y$  of subject  $i$  ( $i = 1, 2, \dots, N$ ) on occasion  $j$  ( $j = 1, 2, \dots, n_i$ )



# The mixed-effects location scale model

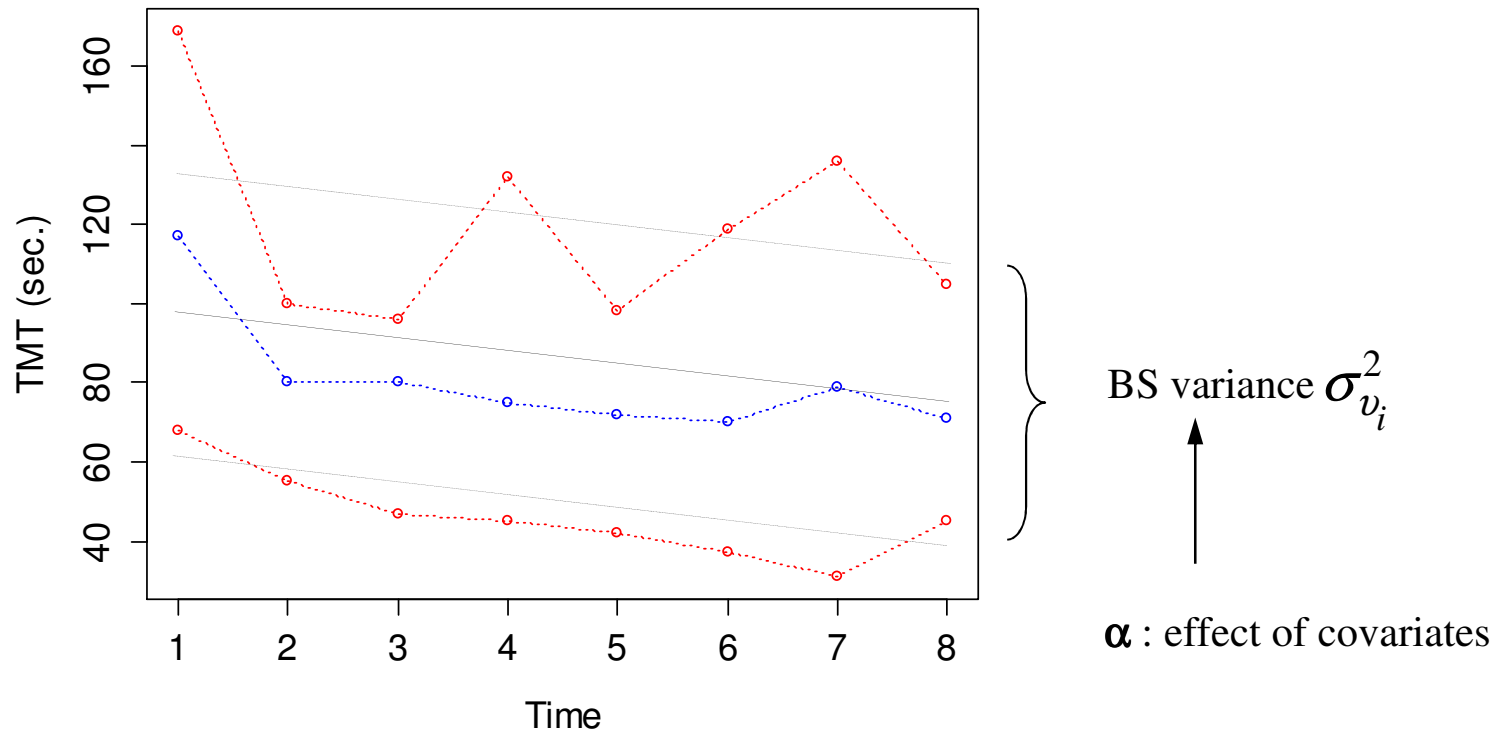
Measurement  $y$  of subject  $i$  ( $i = 1, 2, \dots, N$ ) on occasion  $j$  ( $j = 1, 2, \dots, n_i$ )





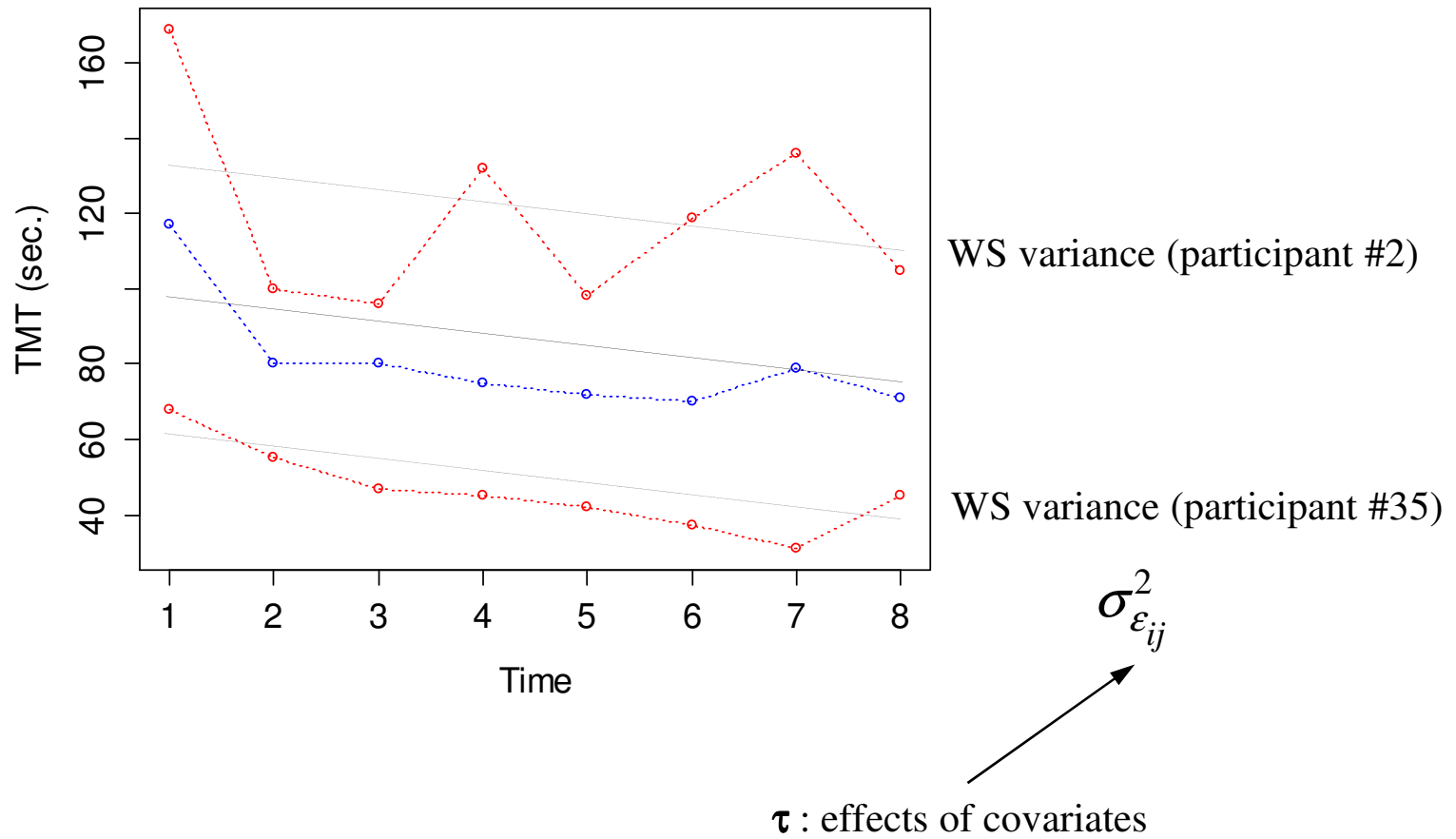
# The mixed-effects location scale model

Measurement  $y$  of subject  $i$  ( $i = 1, 2, \dots, N$ ) on occasion  $j$  ( $j = 1, 2, \dots, n_i$ )



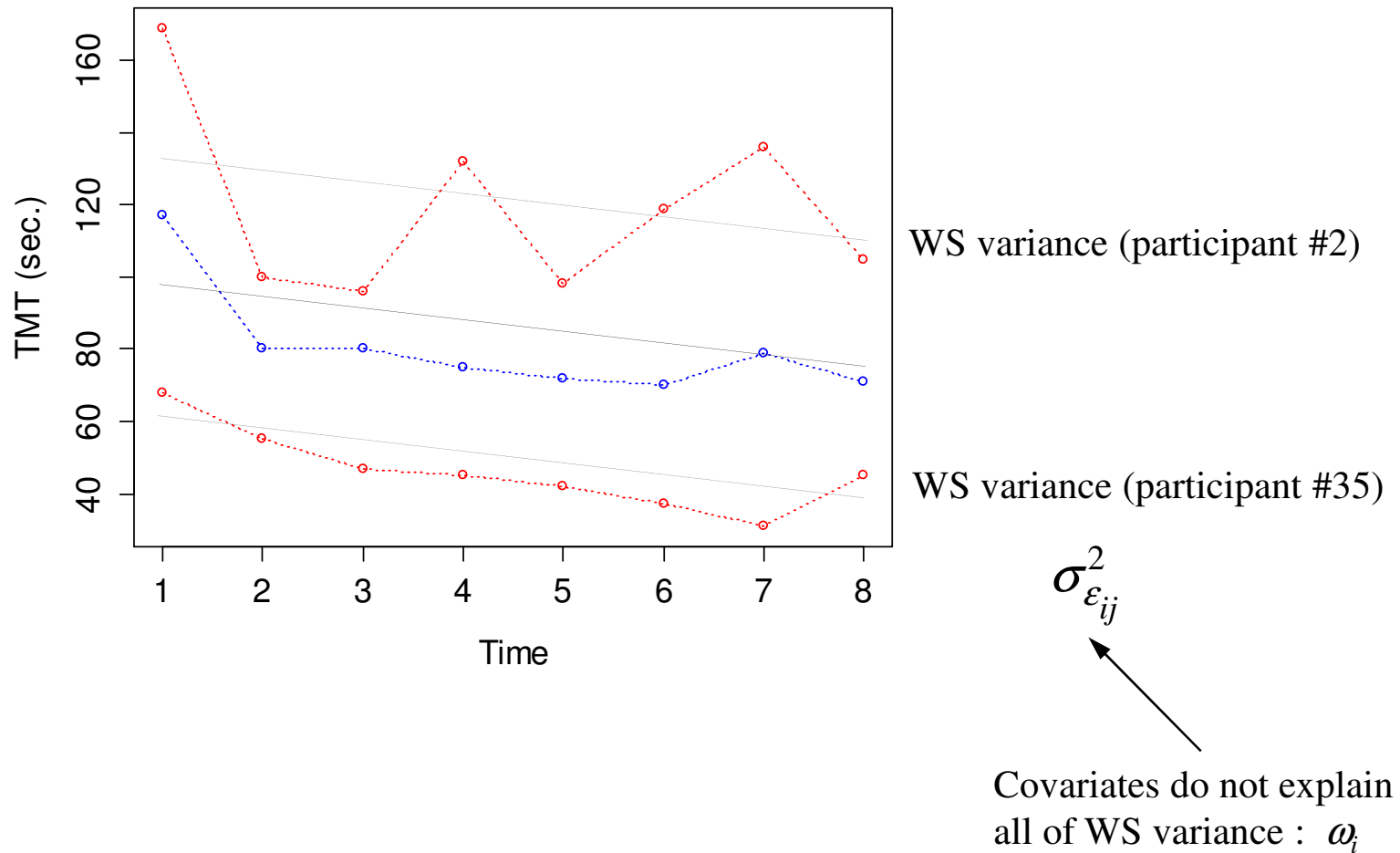
# The mixed-effects location scale model

Measurement  $y$  of subject  $i$  ( $i = 1, 2, \dots, N$ ) on occasion  $j$  ( $j = 1, 2, \dots, n_i$ )



# The mixed-effects location scale model

Measurement  $y$  of subject  $i$  ( $i = 1, 2, \dots, N$ ) on occasion  $j$  ( $j = 1, 2, \dots, n_i$ )



# The mixed-effects location scale model

*EXAMPLE - Analysis of the trail making test performance with random location and scale effects using MIXREGLS (Hedeker & Nordgren, 2013)*

**Model :**  $tmt \sim 1+cov. \mid 1+cov. \mid 1+cov., id="ID"$



**The mean submodel :**

Reference mean :  $\beta_0$

+

$\beta^*$  for covariate  $u^*$

# The mixed-effects location scale model

*EXAMPLE - Analysis of the trail making test performance with random location and scale effects using MIXREGLS (Hedeker & Nordgren, 2013)*

**Model** :  $tmt \sim 1+cov. \mid 1+cov. \mid 1+cov. , id="ID"$



**The BS variance submodel :**

Reference variance :  $\exp(\alpha_0)$  when  $u_j = 0$

+  $\exp(\alpha^*)$  for covariate  $u^*$

# The mixed-effects location scale model

*EXAMPLE - Analysis of the trail making test performance with random location and scale effects using MIXREGLS (Hedeker & Nordgren, 2013)*

**Model :**  $tmt \sim 1+cov. \mid 1+cov. \mid 1+cov., id="ID"$



**The WS variance submodel :**

Reference variance :  $\exp(\tau_0)$  when  $w_{ij} = 0$

+  $\exp(\tau^*)$  for covariate  $w^*$

# The mixed-effects location scale model

*EXAMPLE - Analysis of the trail making test (part B) performance with random location and scale effects using MIXREGLS*

Results :

---

MODEL : tmtb ~1 | 1 | 1, id="id"

---

-2 ln L: 451.560

Variable	Estimate	AsymStdError	z-value	p-value
BETA (regression coefficients)				
Intercept ( $\beta_0$ )	2.232	0.2171	10.283	0.000
ALPHA (BS variance parameters: log-linear model)				
Intercept ( $\alpha_0$ )	0.336	0.2926	1.149	0.251
TAU (WS variance parameters: log-linear model)				
Intercept ( $\tau_0$ )	-1.576	0.226	-6.965	0.000
Influence of the location random effect on the (log of the) WS variance				
$\tau_{linear}$	1.056	0.190	5.553	0.000
Standard deviation of the random subject scale effect				
$\sigma_\omega$	0.347	0.189	1.833	0.067
<hr/>				
BS variance : $\exp(\alpha_0)$	1.399			
WS variance : $\exp(\tau_0 + 0.5 * (\tau_{linear}^2 + \sigma_\omega^2))$	0.369			
ICC = BS/(BS + WS)	0.791			

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# The mixed-effects location scale model

*EXAMPLE - Analysis of the trail making test (part B) performance with random location and scale effects using MIXREGLS*

Results : MODEL : tmtb ~ time | time | 1, id="id"

-2 ln L: 413.792 ; Likelihood ratio test :  $\Delta\chi^2 = 451.60-413.79 =37.81, \Delta df=2$

Variable	Estimate	AsymStdError	z-value	p-value
BETA (regression coefficients)				
Intercept ( $\beta_0$ )	2.489	0.237	10.504	0.000
time ( $\beta_1$ )	-0.080	0.016	-5.147	0.000
ALPHA (BS variance parameters: log-linear model)				
Intercept ( $\alpha_0$ )	0.499	0.301	1.661	0.097
time ( $\alpha_1$ )	-0.056	0.031	-1.776	0.076
TAU (WS variance parameters: log-linear model)				
Intercept ( $\tau_0$ )	-1.727	0.231	-7.466	0.000
Influence of the location random effect on the (log of the) WS variance				
$\tau_{linear}$	1.138	0.184	6.202	0.000
Standard deviation of the random subject scale effect				
$\sigma_\omega$	0.101	0.427	0.237	0.813



# The mixed-effects location scale model

*EXAMPLE - Analysis of the trail making test (part B) performance with random location and scale effects using MIXREGLS*

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Results : MODEL : tmtb ~ time + tmta + age | 1 | age, id="id"

---

-2 ln L: 392.580 ; Likelihood ratio test :  $\Delta\chi^2 = 413.79 - 392.58 = 21.21$ ,  $\Delta df = 2$

Variable	Estimate	AsymStdError	z-value	p-value
BETA (regression coefficients)				
Intercept ( $\beta_0$ )	1.893	0.209	9.053	0.000
time ( $\beta_1$ )	-0.052	0.010	-5.111	0.000
tmta ( $\beta_2$ )	0.693	0.172	4.035	0.000
age ( $\beta_3$ )	0.508	0.157	3.238	0.000
ALPHA (BS variance parameters: log-linear model)				
Intercept ( $\alpha_0$ )	-0.370	0.305	-1.212	0.226
TAU (WS variance parameters: log-linear model)				
Intercept ( $\tau_0$ )	-1.710	0.197	-8.671	0.000
age ( $\tau_3$ )	0.504	0.198	2.547	0.011
Influence of the location random effect on the (log of the) WS variance				
$\tau_{\text{linear}}$	0.955	0.161	5.918	0.000
Standard deviation of the random subject scale effect				
$\sigma_\omega$	0.000	0.215	0.000	1.000

---

# The mixed-effects location scale model

*EXAMPLE - Analysis of AX-CPT reaction time with random location and scale effects using MIXREGLS*

Results : MODEL WITHOUT ANY COVARIATES : tr ~ 1 | 1 | 1, id="id"

---

-2 ln L: -167.264

Variable	Estimate	AsymStdError	z-value	p-value
BETA (regression coefficients)				
Intercept ( $\beta_0$ )	0.629	0.025	25.190	0.000
ALPHA (BS variance parameters: log-linear model)				
Intercept ( $\alpha_0$ )	-3.889	0.252	-15.424	0.000
TAU (WS variance parameters: log-linear model)				
Intercept ( $\tau_0$ )	-3.029	0.177	-17.093	0.000
Influence of the location random effect on the (log of the) WS variance				
$\tau_{linear}$	0.708	0.158	4.494	0.000
Standard deviation of the random subject scale effect				
$\sigma_\omega$	0.851	0.099	8.540	0.000
<hr/>				
BS variance : $\exp(\alpha_0)$	0.020			
WS variance : $\exp(\tau_0 + 0.5 * (\tau_{linear}^2 + \sigma_\omega^2))$	0.089			
ICC = BS / (BS + WS)	0.187			

---

# The mixed-effects location scale model

*EXAMPLE - Analysis of AX-CPT reaction time with random location and scale effects using MIXREGLS*

Results : 

---

MODEL WITH RANDOM SCALE : tr ~ age | 1 | age, id="id"

---

-2 ln L: -178.394, Likelihood ratio test :  $\chi^2_2 = -167.264 + 178.394 = 11.131$

Variable	Estimate	AsymStdEr r	z-value	p-value
BETA (regression coefficients)				
Intercept ( $\beta_0$ )	0.048	0.152	0.317	0.751
age ( $\beta_1$ )	0.008	0.002	3.863	0.000
ALPHA (BS variance parameters: log-linear model)				
Intercept ( $\alpha_0$ )	-4.276	0.259	-16.536	0.000
TAU (WS variance parameters: log-linear model)				
Intercept ( $\tau_0$ )	-5.472	1.295	-4.225	0.000
age ( $\tau_1$ )	0.032	0.016	1.909	0.006
Influence of the location random effect on the (log of the) WS variance				
$\tau_{\text{linear}}$	0.632	0.144	4.386	0.000
Standard deviation of the random subject scale effect				
$\sigma_{\omega}$	0.826	0.089	9.232	0.000

A Bayesian model for estimating intra-individual variability as a predictor

## Statistics from a Bayesian perspective, in a (very) few words...

*Bayesian statistics starts by using (prior) probabilities to describe the current state of knowledge*

The prior distribution represents a specific assumption about a model parameter. It is a distribution of credibility across parameter values  $\theta$  of the model that expresses previous knowledge about the parameter values without the newly collected data :

the prior density  $p(\theta)$

The specification of a very uncertain prior implies that the prior has minimal influence on the estimates of the parameters.

## Statistics from a Bayesian perspective, in a (very) few words...

*Bayesian statistics uses the sampling distribution  $p(y|\theta)$  of the data  $y$  as a function of a model with its parameters  $\theta$*

The likelihood function  $p(y|\theta)$  is the same as the sampling distribution of the observed data  $y$  but read in the opposite way.

The value  $\hat{\theta}$  which yields the maximum of the likelihood function for the observed data  $y$  is called the maximum of the likelihood estimate of the parameter  $\theta$ .

## Statistics from a Bayesian perspective, in a (very) few words...

*Bayesian statistics uses Bayes rule and incorporates information through the collected data*

Bayes rule describes the relationship between the two conditional probabilities  $p(A|B)$  and  $p(B|A)$  :

$$p(A|B) = \frac{p(B|A)p(A)}{p(B)}.$$

Bayes rule is used to derive the probability of the parameters  $\theta$  given the data  $y$ , that is the posterior distribution  $p(\theta|y)$  :

$$p(\theta|y) = \frac{p(y|\theta)p(\theta)}{p(y)}.$$

The marginal density  $p(y)$  is a constant that contains high-dimensional integrals which are often impossible to compute analytically.

# Statistics from a Bayesian perspective, in a (very) few words...

*Bayesian statistics relies on computer simulations that draw samples from the posterior distribution given a model, a likelihood  $p(\theta | y)$ , and data  $y$*

Integration is typically performed by computer simulations :

Let the data be  $y$  and a vector  $\theta = (\theta_1, \theta_2, \dots, \theta_k)$  of  $k$  unknown parameters.

1. Choose initial values  $\theta_1^0, \theta_2^0, \dots, \theta_k^0$
2. Sample  $\theta_1^1$  from  $p(\theta_1 | \theta_2^0, \theta_3^0, \dots, \theta_k^0, y)$   
Sample  $\theta_2^1$  from  $p(\theta_2 | \theta_1^0, \theta_3^0, \dots, \theta_k^0, y)$   
.....  
Sample  $\theta_k^1$  from  $p(\theta_k | \theta_1^0, \theta_2^0, \dots, \theta_{k-1}^0, y)$
3. repeat step 2 very many times (e.g. 50000)

The sequence of random draws for each of  $k$  parameters resulting from step 3 forms a Markov Chain Monte Carlo (MCMC) sample.

If chains are converged, the sample that approximates the posterior is summarized for inference : mean, mode, median, variance, probability interval (e.g., 95% PI) for every parameter.



# **A Bayesian model for estimating intra-individual variability**

*The Bayesian variability model* (Wiley, 2015) :

1. offers unbiased, correct estimates ;
2. gives more effective and more power results with smaller sample sizes ;
3. accounts for systematic changes ;
4. allows for some missing data.

# A Bayesian model for estimating intra-individual variability

## *A two-stage modeling*

1. Estimating intra-individual variability of  $X_{ij}$  (subject  $i$ , occasion  $j$ ) in a mixed-effects regression framework :

$$X_{ij} \sim N(\mu_i, \sigma_i^2).$$

Prior distribution on  $\mu_i$  :  $\mu_i \sim N(\mu_\mu, \sigma_\mu^2)$  ;

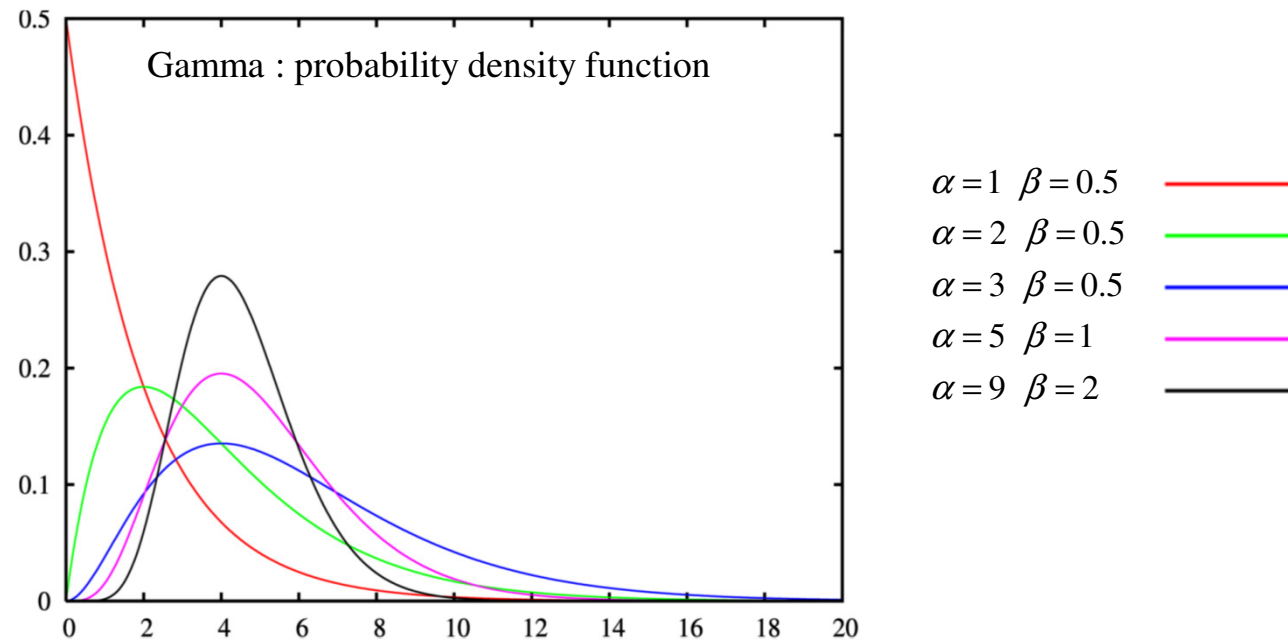
Reference prior on  $\sigma_i^2$  that is independent of  $\mu_i$  :  $\sigma_i^2 \sim \Gamma(\alpha, \beta)$ ,  
with shape and (inverse) scale parameters  $\alpha$  and  $\beta$ .

# A Bayesian model for estimating intra-individual variability

## *A two-stage modeling*

1. Estimating intra-individual variability of  $X_{ij}$  (subject  $i$ , occasion  $j$ ) in a mixed-effects regression framework :

$\sigma_i^2 \sim \Gamma(\alpha, \beta)$ , with shape and (inverse) scale parameters  $\alpha$  and  $\beta$ .



# A Bayesian model for estimating intra-individual variability

*A two-stage modeling*

- Using the estimate of intra-individual variability, accounting for measurement error, as a predictor in a multiple regression framework :

$$Y_i \sim N(\mu_{2i}, \sigma_2),$$

where:

$$\mu_{2i} = \beta_0 + \beta_k \text{Covariates}_k + \underbrace{\alpha_1 \sigma_i + \alpha_2 \mu_i}_{\text{latent (estimated) variables from step 1}}$$

latent (estimated) variables  
from step 1

# A Bayesian model for estimating intra-individual variability

*EXAMPLE - Analysis of the effect of intra-individual variability (TMT part B) on performance on the Frontal Assessment Battery (FAB) using ‘varian’*

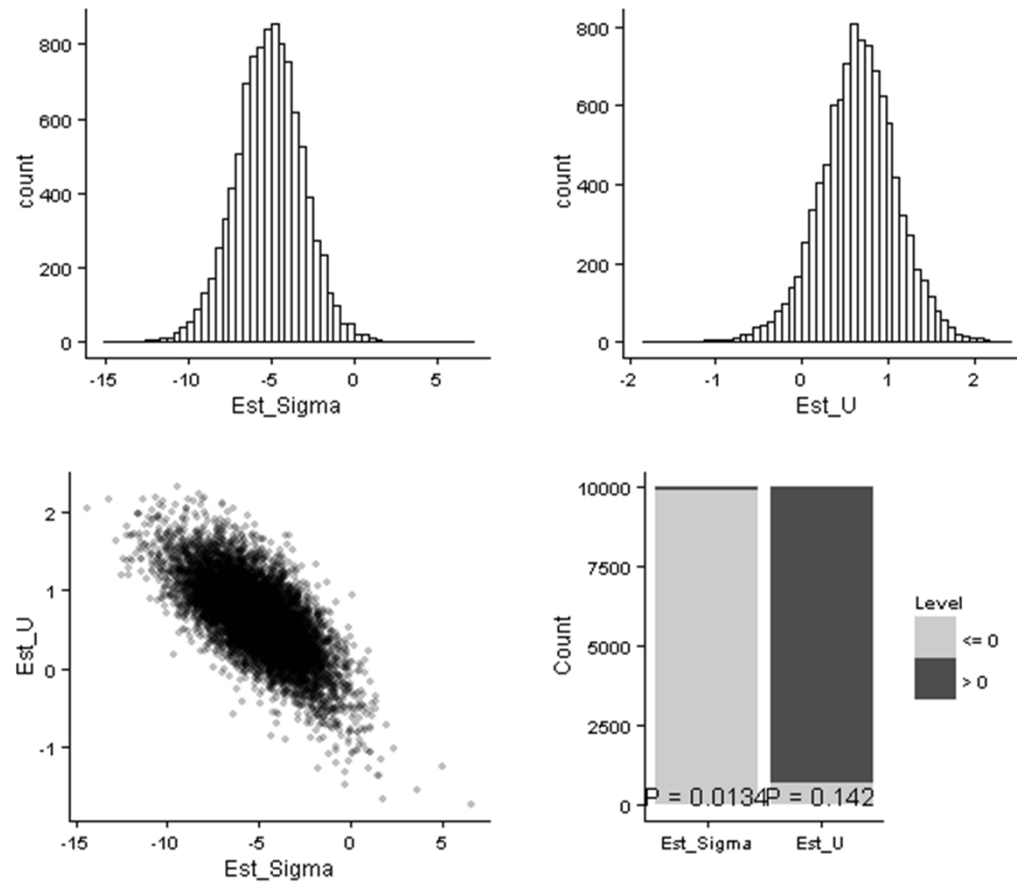
Results :

MODEL			
tmb ~time + tmta + age   ID (linear time detrending)			
var_intra(tmtb) + mean(tmtb) → FAB			
VARIABILITY ANALYSIS			
	Estimate	95% CI	p-value
<b>TMT.B</b>			
intercept	2.01	[1.84, 2.52]	0.000
time	-0.05	[-0.07, -0.03]	0.000
tmta	0.54	[0.39, 0.99]	0.013
age	0.55	[0.42, 0.92]	0.001
$\sigma_\mu$	1.01	[0.72, 1.38]	0.000
gamma shape	3.91	[2.11, 6.60]	0.000
gamma rate	8.01	[4.02,13.92]	0.000
average ISD ( $\alpha/\beta$ )	0.49		
<b>FAB</b>			
intercept	18.96	[16.92, 21.01]	0.000
$\alpha_1$ : var_intra(tmtb)	-5.12	[-9.20, -1.19]	0.013
$\alpha_2$ : mean(tmtb)	0.65	[-0.29, 1.53]	0.142
residual	1.35	[0.67, 1.99]	0.000

# A Bayesian model for estimating intra-individual variability

*EXAMPLE - Analysis of the effect of intra-individual variability (TMT part B) on performance on the Frontal Assessment Battery (FAB) using 'varian'*

Results :



# A Bayesian model for estimating intra-individual variability

*EXAMPLE - Analysis of the effect of intra-individual variability (TMT part B) on performance on the Frontal Assessment Battery (FAB) using ‘varian’*

Results :

random effects

$\mu_i$				$\sigma_i$				
ID	est.	2.5%	97.5%	ID	est.	2.5%	97.5%	Raw ISD
1	0.88	[	0.38 , 1.40 ]	1	0.38	[	0.24 , 0.59 ]	0.35
2	0.01	[	-0.66 , 0.68 ]	2	0.63	[	0.44 , 0.91 ]	0.72
3	-0.46	[	-0.97 , 0.06 ]	3	0.41	[	0.22 , 0.69 ]	0.31
4	2.10	[	1.31 , 2.89 ]	4	0.85	[	0.62 , 1.19 ]	1.19
5	0.04	[	-0.51 , 0.59 ]	5	0.39	[	0.24 , 0.63 ]	0.45
6	-0.09	[	-0.62 , -0.04 ]	6	0.50	[	0.27 , 0.83 ]	0.30
...	...	[	... ]	...	...	[	... ]	...

# A Bayesian model for estimating intra-individual variability

*EXAMPLE - Analysis of the effect of intra-individual reaction time variability (AX-CPT paradigm) on performance on the Frontal Assessment Battery (FAB) using ‘varian’*

Results :

MODEL			
axcpt ~1  ID			
axcpt_var+axcpt_mean → FAB			
VARIABILITY ANALYSIS			
	Estimate	95% CI	p-value
AX-CPT			
intercept	0.62	[0.57, 0.67]	0.000
$\sigma_{\mu}$	0.14	[0.11, 0.19]	0.000
gamma shape	3.18	[1.93, 4.77]	0.000
gamma rate	12.24	[7.07, 18.98]	0.000
average ISD ( $\alpha/\beta$ )	0.26		
FAB			
intercept	16.84	[15.46, 18.21]	0.000
$\alpha_1$ : var_intra(tmtb)	-1.98	[-6.60, 2.62]	0.387
$\alpha_2$ : mean(tmtb)	-1.55	[-7.30, 4.23]	0.594
residual	1.87	[1.46, 2.44]	0.000



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