Modeling Mood Variation and Covariation among Adolescent Smokers: Application of a Bivariate Location-Scale Mixed-Effects Model

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Outline

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- Objectives
- Model and Its Estimation
- Data Analysis Results
- Conclusions

Motivation

1. Heterogeneous within- and between-subject (WS and BS) variances in longitudinal or clustered data

2. Multiple outcomes in behavioral, social, and medical studies

3. Ecological Momentary Assessment (EMA) data collection produces many observations per subject

Objective

- Specify a joint model for two continuous outcomes with heterogeneous WS and BS variances
  - Two outcomes are modeled by mixed-effects regression models with random intercepts
  - BS variance is modeled as heterogeneous between subjects
  - WS variance is modeled as heterogeneous with random scale effects
  - BS and WS covariances are modeled with their own set of covariates

Model in Matrix Form

$$\boldsymbol{Y}_i = \boldsymbol{X}_i\boldsymbol{\beta} + \boldsymbol{Z}_i\boldsymbol{u}_i + \boldsymbol{\varepsilon}_i$$ model for the means

$$\sigma^2_{u_i^{(k)}} = \exp\left((\boldsymbol{V}_i^{(k)})^T \tau^{(k)}\right), \; k = 1,2$$ model for BS variances

$$\sigma_{u_i^{(1)}u_i^{(2)}} = \left(\boldsymbol{V}_i^{(12)}\right)^T \boldsymbol{\tau}^{(12)}$$ model for BS covariance

$$\sigma^2_{\varepsilon_{ij}^{(k)}} = \exp\left((\boldsymbol{W}_{ij}^{(k)})^T \boldsymbol{\gamma}^{(k)} + \omega_i^{(k)}\right), \; k = 1,2$$ model for WS variances

$$\sigma_{\varepsilon_{ij}^{(1)}\varepsilon_{ij}^{(2)}} = (\boldsymbol{W}_{ij}^{(12)})^T \boldsymbol{\gamma}^{(12)}$$ model for WS covariance

$$\begin{bmatrix} \boldsymbol{u}_i \\ \boldsymbol{\omega}_i \end{bmatrix} \sim N\left(0, \; \boldsymbol{G}_i\right);$$

$$\boldsymbol{\varepsilon}_i \,\middle|\, \boldsymbol{u}_i, \boldsymbol{\omega}_i = \begin{bmatrix} \varepsilon_{i1}^{(1)} \middle| u_i^{(1)}, \omega_i^{(1)} \\ \varepsilon_{i2}^{(1)} \middle| u_i^{(1)}, \omega_i^{(1)} \\ \cdots \\ \varepsilon_{in_i}^{(2)} \middle| u_i^{(2)}, \omega_i^{(2)} \end{bmatrix} \sim N\left(0, \Sigma_i(\boldsymbol{\omega}_i)\right)$$

j − observation; i − subject

Model - Means

General bivariate mixed-effects model with random intercepts

$$\begin{bmatrix} \boldsymbol{Y}_i^{(1)} \\ \boldsymbol{Y}_i^{(2)} \end{bmatrix} = \begin{bmatrix} \boldsymbol{X}_i^{(1)} & 0 \\ 0 & \boldsymbol{X}_i^{(2)} \end{bmatrix} \begin{bmatrix} \boldsymbol{\beta}^{(1)} \\ \boldsymbol{\beta}^{(2)} \end{bmatrix} + \begin{bmatrix} 1_{\boldsymbol{n}_i} & 0 \\ 0 & 1_{\boldsymbol{n}_i} \end{bmatrix} \begin{bmatrix} u_i^{(1)} \\ u_i^{(2)} \end{bmatrix} + \begin{bmatrix} \boldsymbol{\varepsilon}_i^{(1)} \\ \boldsymbol{\varepsilon}_i^{(2)} \end{bmatrix}$$

$X_i^{(k)}$ - $n_i \times p^{(k)}$ design matrix

$\beta^{(k)}$ - $p^{(k)}$ vector of fixed effect parameters

$u_i^{(k)}$ - individual random effect, k=1,2

$$\begin{bmatrix} \boldsymbol{u}_i \\ \boldsymbol{\omega}_i \end{bmatrix} \sim N\left(0, \quad \boldsymbol{G}_i\right); \qquad \begin{bmatrix} \varepsilon_{ij}^{(1)} \middle| u_i^{(1)}, \omega_i^{(1)} \\ \varepsilon_{ij}^{(2)} \middle| u_i^{(2)}, \omega_i^{(2)} \end{bmatrix} \sim N\left(0, \Sigma_{ij}(\boldsymbol{\omega}_i)\right)$$

Model - WS variance-covariance

$$\Sigma_{ij}(\boldsymbol{\omega}_i) = \begin{bmatrix} \sigma^2_{\varepsilon^{(1)}_{ij}} & \sigma_{\varepsilon^{(1)}_{ij}\varepsilon^{(2)}_{ij}} \\ \sigma_{\varepsilon^{(1)}_{ij}\varepsilon^{(2)}_{ij}} & \sigma^2_{\varepsilon^{(2)}_{ij}} \end{bmatrix}$$

Variance-covariance matrix of *(ij)*th error vector

$$\sigma^2_{\varepsilon^{(k)}_{ij}} = \exp\left((\boldsymbol{W}^{(k)}_{ij})^T \boldsymbol{\gamma}^{(k)} + \omega^{(k)}_i\right), \ k = 1, 2$$

$$\sigma_{\varepsilon^{(1)}_{ij}\varepsilon^{(2)}_{ij}} = (\boldsymbol{W}^{(12)}_{ij})^T \boldsymbol{\gamma}^{(12)}$$

$W^{(k)}_{ij}, W^{(12)}_{ij}$ - vector of covariates for WS variances and covariance

$\gamma^{(k)}, \gamma^{(12)}$ - vector of parameters for WS variances and covariance

$\omega^{(k)}$ - vector of random scale effects

Model - WS variance-covariance

Since random scale has Normal distribution

$$\omega^{(k)} \sim N(0; \sigma^2_{\omega_i^{(k)}}),\ \ k = 1, 2$$

and WS variance is modeled as log-linear model

$$\sigma^2_{\varepsilon_{ij}^{(k)}} = \exp\left((\boldsymbol{W}_{ij}^{(k)})^T \boldsymbol{\gamma}^{(k)} + \omega_i^{(k)} \right),\ \ k = 1, 2$$

Then WS variance has log-Normal distribution

$$\sigma^2_{\varepsilon_{ij}^{(k)}} \sim \log N\left((\boldsymbol{W}_{ij}^{(k)})^T \boldsymbol{\gamma}^{(k)},\ \sigma^2_{\omega_i^{(k)}} \right),\ \ k = 1, 2$$

Model – BS variance-covariance

Random location-scale effects:

$$\begin{bmatrix} u_i^{(1)} \\ u_i^{(2)} \\ \omega_i^{(1)} \\ \omega_i^{(2)} \end{bmatrix} \sim N\left(0, \quad \boldsymbol{G}_i\right); \qquad \boldsymbol{G}_i = \left[\begin{array}{cc:cc} \sigma^2_{u_i^{(1)}} & \sigma_{u_i^{(1)}u_i^{(2)}} & \sigma_{u^{(1)}\omega^{(1)}} & \sigma_{u^{(1)}\omega^{(2)}} \\ \sigma_{u_i^{(1)}u_i^{(2)}} & \sigma^2_{u_i^{(2)}} & \sigma_{u^{(2)}\omega^{(1)}} & \sigma_{u^{(2)}\omega^{(2)}} \\ \hdashline \sigma_{u^{(1)}\omega^{(1)}} & \sigma_{u^{(2)}\omega^{(1)}} & \sigma^2_{\omega^{(1)}} & \sigma_{\omega^{(1)}\omega^{(2)}} \\ \sigma_{u^{(1)}\omega^{(2)}} & \sigma_{u^{(2)}\omega^{(2)}} & \sigma_{\omega^{(1)}\omega^{(2)}} & \sigma^2_{\omega^{(2)}} \end{array}\right]$$

$$\sigma^2_{u_i^{(k)}} = \exp\left((\boldsymbol{V}_i^{(k)})^T \tau^{(k)} \right), \;\; k = 1,2$$

$$\sigma_{u_i^{(1)}u_i^{(2)}} = \left(\boldsymbol{V}_i^{(12)}\right)^T \boldsymbol{\tau}^{(12)}$$

$V_i^{(k)}, V_i^{(12)}$-vector of covariates for BS variances and covariance

$\tau^{(k)}, \tau^{(12)}$ - vector of parameters for BS variances and covariance

Model Estimation

Given the above assumptions, the conditional distribution of the outcomes given random location and scale effects is

$$\boldsymbol{Y}_i \left| \boldsymbol{u}_i, \boldsymbol{\omega}_i \sim N(\boldsymbol{X}_i \boldsymbol{\beta} + \boldsymbol{Z}_i \boldsymbol{u}_i,\ \Sigma_i(\boldsymbol{\omega}_i)) \right.$$

The full likelihood for all subjects in the sample is

$$\prod_{i=1}^{N} f\left(\boldsymbol{Y}_i \left| \boldsymbol{u}_i, \boldsymbol{\omega}_i, \boldsymbol{\theta} \right.\right) g(\boldsymbol{u}_i, \boldsymbol{\omega}_i)$$

where $\boldsymbol{\theta} = (\boldsymbol{\beta}^T, \boldsymbol{\gamma}^T, \boldsymbol{\tau}^T)^T$

The marginal likelihood is obtained by integrating out all random effects from the full likelihood.

$$h(\boldsymbol{Y}_i) = \int_{\boldsymbol{u},\boldsymbol{\omega}} f\left(\boldsymbol{Y}_i \left| \boldsymbol{u}, \boldsymbol{\omega} \right.\right) g(\boldsymbol{u}, \boldsymbol{\omega}) \partial \boldsymbol{u} \partial \boldsymbol{\omega}$$

The model was estimated in PROC NLMIXED, SAS v9.2

Data Description

Data used in the analysis is part of a larger longitudinal natural history study of adolescent smoking

- EMA baseline data based on random prompts
- 461 students, 9^{th} and 10^{th} grades
- 30 prompts per student on average, range 7-71
- 14,105 prompts total

<u>Outcomes:</u>

- Positive Affect (PA)
- Negative Affect (NA)

<u>Covariates:</u>

- Smoking level, represented by a number of smoking events during EMA
  - Non-smokers to one-cigarette smokers
  - Slope among smokers

Descriptive Statistics

Variable	Mean	Std	Min	Max
Positive Affect (PA)	6.80	1.93	1	10
Negative Affect (NA)	3.46	2.25	1	10
Age	15.67	0.61	13.85	17.29
Gender (Male)	44.9%			
School grade (9th grade)	50.7%			
White	56.8%			
African American	15.8%			
Latino	20.0%			
Asian/Pacific	2.8%			
Smoking level				
At least one smoking event	50.8%			
One smoking event among smokers	24.8%			
Smoking episodes on EMA among smokers	5		1	42

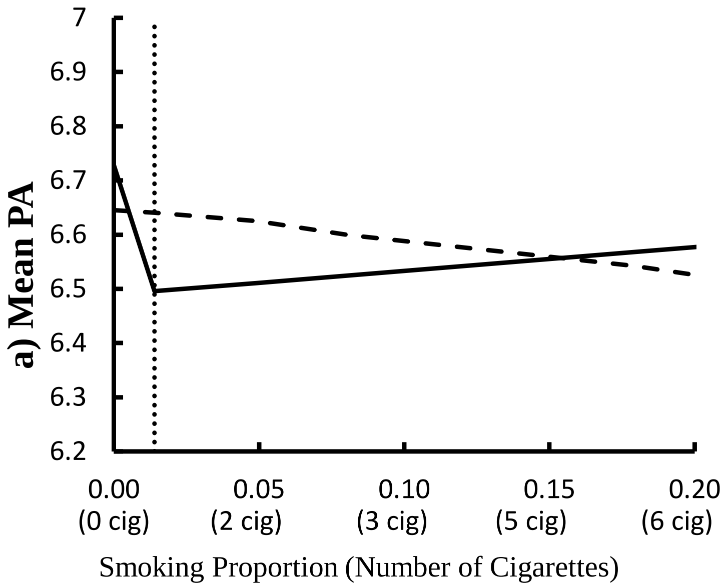
Bivariate location-scale mixed-effects model of PA and NA with piecewise smoking predictor

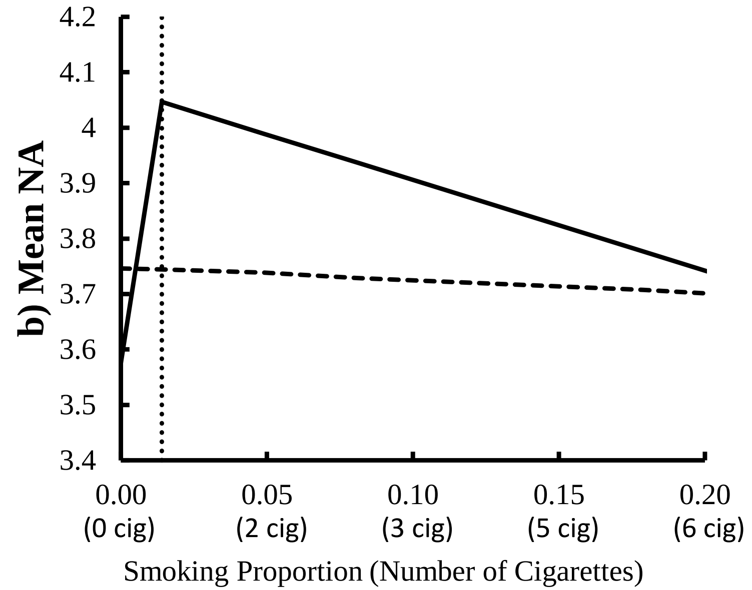
N subject=461, N observations=14,105

		Positive Affect			Negative Affect		
Model	Parameter	Estimate	Std Err	p	Estimate	Std Err	p
Fixed Effect covariates							
	Intercept	6.729	0.116	<.0001	3.576	0.137	<.0001
	Male	**0.299**	**0.111**	**0.0075**	**-0.586**	**0.135**	**<.0001**
	10th grade	0.013	0.113	0.9098	0.057	0.135	0.6716
	1-cig smoker	-0.233	0.136	0.0885	**0.471**	**0.167**	**0.0050**
	Amount smoked	0.437	0.676	0.5184	**-1.637**	**0.766**	**0.0332**
WS variance							
	Intercept	0.856	0.049	<.0001	0.961	0.060	<.0001
	Male	**-0.247**	**0.049**	**<.0001**	**-0.418**	**0.060**	**<.0001**
	10th grade	**-0.144**	**0.049**	**0.0033**	-0.092	0.059	0.1226
	1-cig smoker	0.115	0.059	0.0504	**0.353**	**0.072**	**<.0001**
	Amount smoked	**-0.597**	**0.295**	**0.0439**	**-1.395**	**0.359**	**0.0001**
BS variance							
	Intercept	0.260	0.090	0.0042	0.654	0.086	<.0001
	Male	-0.173	0.120	0.1507	**-0.369**	**0.117**	**0.0017**
	10th grade	-0.179	0.116	0.1227	0.188	0.111	0.0915
	1-cig smoker	0.109	0.145	0.4538	0.202	0.136	0.1373
	Amount smoked	-0.104	0.803	0.8968	-0.907	0.610	0.1375
Random scale variance on log scale		**-1.637**	**0.085**	**<.0001**	**-1.119**	**0.083**	**<.0001**
Exp(variance)		0.195			0.327		

Estimated mean PA (a) and mean NA (b) for different smoking level

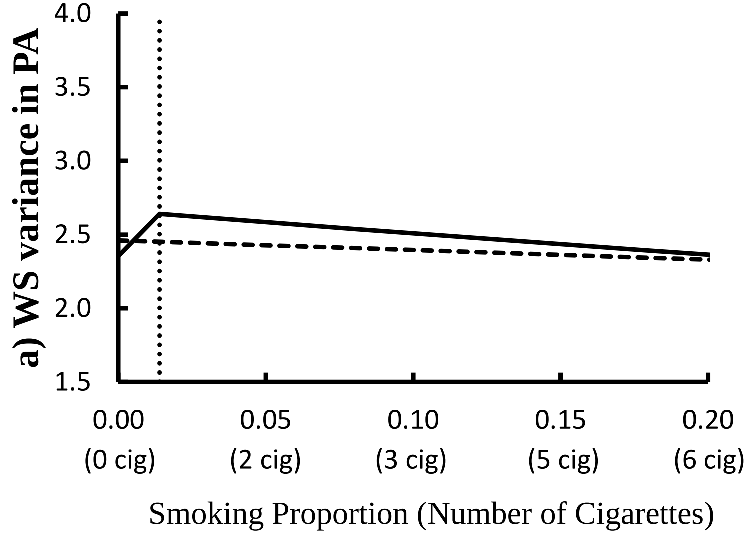
Solid line - piecewise smoking;
Dashed line – continuous smoking;
Dotted vertical line – break-point in the slope of smoking effect, occurred at 0.014 smoking proportion (1 cigarette)

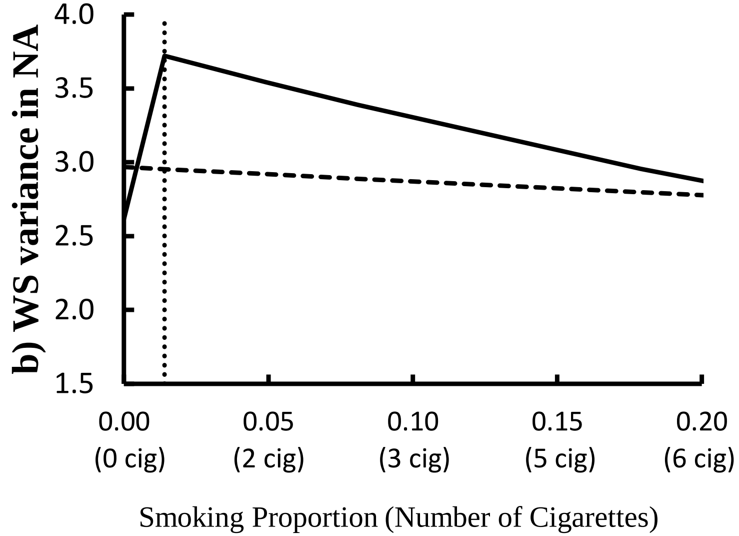




Estimated WS PA and NA variance for different smoking level

Solid line - piecewise smoking;
Dashed line – continuous smoking;
Dotted vertical line – break-point in the slope of smoking effect, occurred at 0.014 smoking proportion (1 cigarette)





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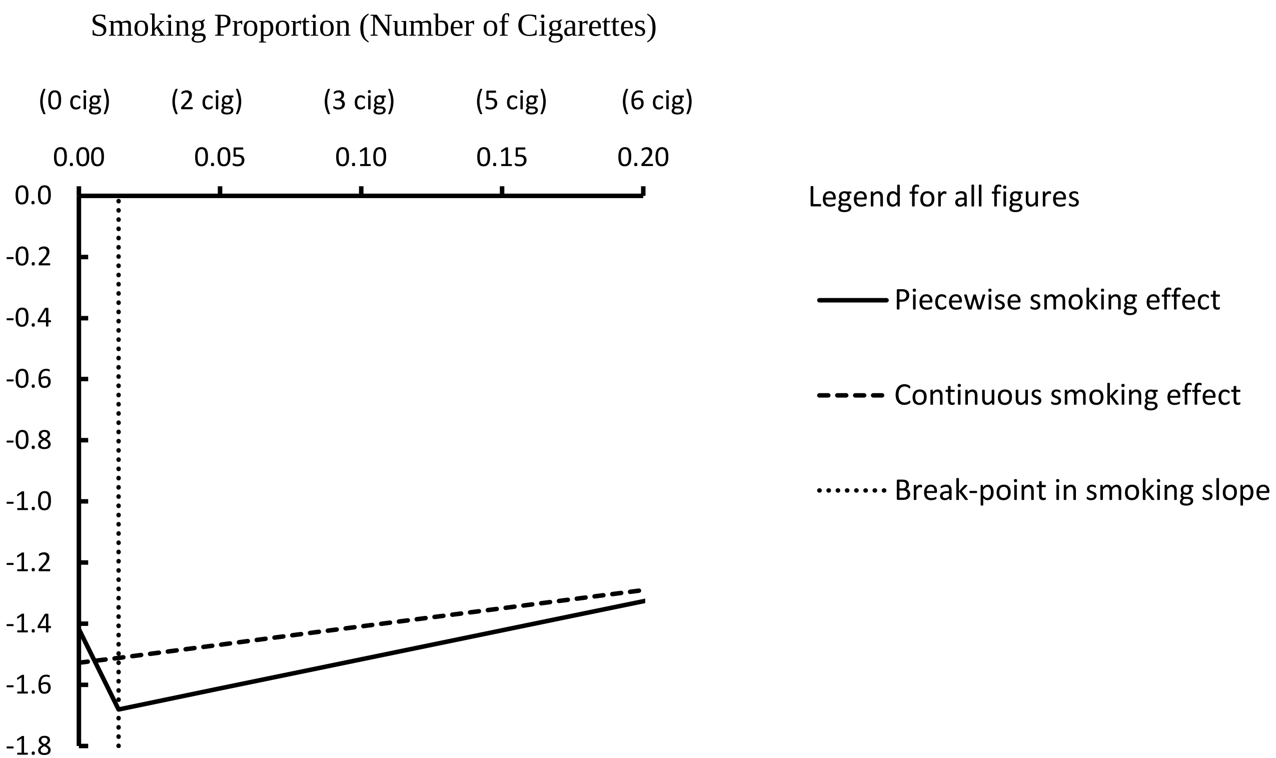
Bivariate location-scale mixed-effects model of PA and NA with piecewise smoking predictor

N subject=461, N observations=14,105

Sub-model	Parameter	Estimate	Std Err	p
WS covariance				
	Intercept	**-1.417**	**0.049**	**<.0001**
	Male	**0.607**	**0.044**	**<.0001**
	10th grade	**0.210**	**0.043**	**<.0001**
	1-cig smoker	**-0.263**	**0.053**	**<.0001**
	Amount smoked	**1.900**	**0.206**	**<.0001**
BS covariance				
	Intercept	**-0.901**	**0.115**	**<.0001**
	Male	0.293	0.156	0.0621
	10th grade	-0.190	0.146	0.1932
	1-cig smoker	-0.249	0.193	0.1961
	Amount smoked	1.258	0.783	0.1088
Random location (u) and random scale (ω) covariance				
	$\sigma_{\omega^{(PA)}\omega^{(NA)}}$	0.030	0.016	0.0586
	$\sigma_{u^{(PA)}\omega^{(PA)}}$	**-0.175**	**0.030**	**<.0001**
	$\sigma_{u^{(NA)}\omega^{(PA)}}$	0.018	0.034	0.6022
	$\sigma_{u^{(PA)}\omega^{(NA)}}$	**-0.229**	**0.035**	**<.0001**
	$\sigma_{u^{(NA)}\omega^{(NA)}}$	**0.401**	**0.044**	**<.0001**

Estimated WS covariance between PA and NA for different smoking level



Summary

A bivariate mixed-effects model was developed and applied to assess jointly positive and negative moods as a function of smoking level in youth

- Model specified heterogeneous WS and BS variances
- WS and BS covariances were modeled in terms of covariates
- WS variance specification had random scale effects

Thank you!