

Appendix 1 to Rappaport LM, Russell JJ, Hedeker D, Pinard G, Bleau P, Moskowitz DS. Affect, interpersonal behavior and interpersonal perception during open-label, uncontrolled paroxetine treatment of people with social anxiety disorder: a pilot study. *J Psychiatry Neurosci* 2018.

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Design

Participants received \$20 compensation after participation in the 7-day pre-treatment baseline ECR period, \$150 after 8 weeks of treatment, and an additional \$150 at the last session following 16 weeks of treatment.

Data analysis

For growth curve models of change in symptom severity and spin, higher-order polynomials were added successively as fixed then random effects to best model change over time.

Drawn from Hedeker and Mermelstein (2012), 3-level Location-Scale models were run using maximum likelihood estimation with adaptive Gaussian-Hermite quadrature with at least 3 quadrature points. Higher-order polynomials were added successively to best model change in mean level (i.e., location) and intraindividual variability (i.e., variance, scale) over time. Random effects were subsequently added to evaluate inter-individual heterogeneity in mean level and intraindividual variability at baseline and in the trajectory of mean level. Mixed effects models are limited in producing standardized estimates. Instead, unstandardized estimates are presented with 95% confidence intervals.

Each variable is distributed as $N(y_{ijk}, \sigma_{ijk}^2)$ for observation k in wave j for person i .

Fixed Effects:

$$y_{ijk} = (\beta_0 + v_{0i} + v_{0ij}) + (\beta_1 + v_{1i}) * Session_{ij} + \beta_2 * Session_{ij}^2 + \beta_3 * Session_{ij}^3 + \epsilon_{ijk}$$

$$\sigma_{ijk}^2 = \exp(\tau_0 + \tau_1 * Session_{ij} + \omega_i)$$

Random Effects:

$$v_{0i}, v_{0ij}, v_{1i}, \omega_i \sim N \left(0, \begin{pmatrix} \sigma_{v_0}^2 & 0 & \sigma_{v_0 v_1} & \sigma_{v_0 \omega} \\ 0 & \sigma_{v_0}^2 \wedge wave & 0 & 0 \\ \sigma_{v_0 v_1} & 0 & \sigma_{v_1}^2 & 0 \\ \sigma_{v_0 \omega} & 0 & 0 & \sigma_{\omega}^2 \end{pmatrix} \right)$$

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Example code:

```
PROC NL MIXED data=ECR MAXITER=1000 GCONV=1e-12 EBOPT ITDETAILS;
  BOUNDS v0 vs vwave v1 > 0;
  mean = (b0 + u0) + (b1 + u1)*Session + b2*Sessionq
        + d1*w1 + d2*w2 + d3*w3 + d4*w4 + d5*w5;
  vare = EXP(t0 + t1*Session + omega);
  MODEL MNAFXINT ~ NORMAL(mean,vare);
  RANDOM u0 u1 omega d1 d2 d3 d4 d5 ~ NORMAL([0,0,0,0,0,0,0],
        [v0,
        c01,v1,
        c0s,0,vs,
        0,0,0,vwave,
        0,0,0,0,vwave,
        0,0,0,0,0,vwave,
        0,0,0,0,0,0,vwave,
        0,0,0,0,0,0,0,vwave]) SUBJECT=ID;
  PREDICT mean out=NAmean;
  PREDICT vare out=NAvare;
  TITLE '3-level location-scale model for Negative Affect';
run;
```

Results

Change in Symptoms. Two items on the SIAS are reverse-coded. Internal consistency was high at each time point when the 2 reverse-coded items are included ($\alpha = 0.86 - 0.91$) or excluded ($\alpha = 0.85 - 0.91$). Additionally, a univariate growth curve was fit to model change in SIAS symptom severity when computed with the 2 reverse-coded items. Anxiety, as indexed by the SIAS total score, decreased in a monotonically downward pattern, $B_{linear\ slope} = -18.80$, 95% CI [-22.62, -14.98], $p < 0.0001$, with deceleration over time, $B_{quadratic\ slope} = 2.05$, 95% CI [1.45, 2.65], $p < 0.0001$. Results were highly similar to those based on the SIAS total score excluding the 2 reverse-coded items, which are presented in the text.

Correlates of Anxiety Symptomatology. Anxiety symptoms were assessed monthly, prior to each ECR period. Higher anxiety symptom severity was associated with higher mean negative affect, higher submissive behavior, lower dominant behavior, and lower perception of warmth in others' behavior during the following week (see Supplemental Tables 4 & 5, Within-Person).

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Additionally, higher anxiety symptom severity was associated with greater intraindividual variability in negative affect, submissive behavior, and perception of warmth in others' behavior. Associations were consistent across at least 2 of 3 self- and clinician-reported assessments included in the study. Person-level results suggest that, after removing change over time, participants who, over the course of the study, reported higher average anxiety symptom severity also demonstrated, on average, higher negative affect, lower dominant behavior, and higher submissive behavior along with greater intraindividual variability in negative affect (see Supplemental Tables 4 & 5, Between-Person).

Supplemental Table 1. Change in Anxiety and Depressive Symptom Severity over Treatment

	<i>Fixed Effects</i>		<i>Random Effects</i>
	<i>B</i>	<i>CI</i>	<i>Variance (σ^2)</i>
<u>LSAS</u>			
Intercept	116.38 ^	(106.31, 126.45)	185.21
Linear Slope	-35.52 ^	(-43.06, -27.97)	21.37
Quadratic Slope	4.03 ^	(2.81, 5.25)	--
<u>SPS</u>			
Intercept	61.85 ^	(55.65, 68.05)	190.38 ***
Linear Slope	-18.26 ^	(-22.19, -14.33)	14.00 **
Quadratic Slope	2.01 ^	(1.39, 2.63)	--
<u>SIAS</u>			
Intercept	63.96 ^	(59.16, 68.76)	43.76 *
Linear Slope	-17.67 ^	(-21.34, -14.01)	10.89 **
Quadratic Slope	1.92 ^	(1.34, 2.50)	--
<u>MADRS</u>			
Intercept	9.74 ^	(6.91, 12.57)	5.49 *
Linear Slope	-3.07 **	(-5.25, -0.89)	--
Quadratic Slope	0.34	(-0.02, 0.70)	--

Note. LSAS = Liebowitz Social Anxiety Scale; SPS = Social Phobia; SIAS = Social Interaction and Anxiety Scale; MADRS = Montgomery-Åsberg Depression Rating Scale; CI = 95% Confidence Interval. * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, ^ $p \leq 0.0001$.

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Supplemental Table 2. Change in Affect (Positive and Negative) and Perception (Warmth and Dominance) Mean (i.e., Location) and Variance (i.e., Scale) over Treatment

	Positive Affect		Negative Affect	
Mean	B/σ^2	CI	B/σ^2	CI
Intercept	2.21 [^]	(1.89, 2.52)	1.32 [^]	(1.12, 1.51)
Linear Slope	0.47 [^]	(0.29, 0.65)	-0.51 [^]	(-0.62, -0.39)
Quad Slope	-0.08 ^{***}	(-0.13, -0.04)	0.08 [^]	(0.06, 0.11)
σ^2_{int}	0.96 [^]	--	0.36 [^]	--
$\sigma^2_{betweenWave}$	0.14 [^]	--	0.05 [^]	--
σ^2_{slope}	0.04 [*]	--	0.02 ^{**}	--
COV _{int, slope}	0.004	--	-0.05 [*]	--
Variance	B/σ^2	CI	B/σ^2	CI
Intercept	0.18	(-0.01, 0.37)	-0.18	(-0.49, 0.13)
Linear Slope	-0.15 [^]	(-0.19, -0.11)	-0.47 [^]	(-0.51, -0.44)
σ^2_{scale}	0.36 [^]	--	1.07 [^]	--
COV _{int, scale}	0.06	--	0.44 [^]	--
	Perception of Warmth		Perception of Dominance	
Mean	B/σ^2	CI	B/σ^2	CI
Intercept	7.39 [^]	(7.02, 7.75)	7.63 [^]	(7.37, 7.88)
Linear Slope	0.67 [^]	(0.41, 0.93)	--	--
Quad Slope	-0.10 ^{**}	(-0.16, -0.04)	--	--
σ^2_{int}	1.11 ^{***}	--	0.57 ^{***}	--
$\sigma^2_{betweenWave}$	0.15 [*]	--	0.37 [^]	--
σ^2_{slope}	0.08 [*]	--	--	--
COV _{int, slope}	-0.13	--	--	--
Variance	B/σ^2	CI	B/σ^2	CI
Intercept	1.76 [^]	(1.56, 1.97)	1.56 [^]	(1.36, 1.77)
Linear Slope	-0.18 [^]	(-0.22, -0.14)	-0.23 [^]	(-0.27, -0.19)
σ^2_{scale}	0.41 [^]	--	0.39 [^]	--

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COV_{int, scale} -0.33** -- -0.19* --

Note. σ^2_{int} = variance between persons in intercept of the mean; $\sigma^2_{betweenWave}$ = variance within persons between assessments waves (i.e., months); σ^2_{slope} = variance between persons in linear slope over time; COV_{int, slope} = covariance of between persons random intercept and slope; σ^2_{scale} = variance between persons in intercept of the variance; COV_{int, scale} = covariance of between persons random intercept for mean with random intercept for the variance; CI = 95% Confidence Interval. * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, ^ $p \leq 0.0001$.

Supplemental Table 3. Change in Communal and Agentic Behavior Mean (i.e., Location) and Variance (i.e., Scale) over Treatment

	Agreeable Behavior		Quarrelsome Behavior	
Mean	B/σ^2	CI	B/σ^2	CI
Intercept	11.83 [^]	(9.36, 14.29)	-15.21 [^]	(-17.58, -12.83)
Linear Slope	5.22 [^]	(2.94, 7.51)	-1.82*	(-3.47, -0.17)
Quad Slope	-1.06***	(-1.62, -0.50)	0.40*	(-0.003, 0.81)
σ^2_{int}	40.99**	--	46.77***	--
$\sigma^2_{betweenWave}$	7.85	--	2.97	--
σ^2_{slope}	4.38	--	0.70	--
COV _{int, slope}	1.10	--	-0.59	--
Variance	B/σ^2	CI	B/σ^2	CI
Intercept	6.3- [^]	(6.22, 6.39)	6.00 [^]	(5.84, 6.16)
Linear Slope	-0.05**	(-0.08, -0.01)	-0.09 [^]	(-0.13, -0.06)
σ^2_{scale}	0.03*	--	0.23***	--
COV _{int, scale}	-0.65*	--	1.46*	--
	Dominant Behavior		Submissive Behavior	
Mean	B/σ^2	CI	B/σ^2	CI
Intercept	-0.88	(-3.68, 1.92)	3.83*	(0.47, 7.18)
Linear Slope	2.21 [^]	(1.27, 3.15)	-14.28 [^]	(-20.05, -8.51)
Quad Slope	--	--	6.18**	(2.45, 9.91)
Cubic Slope	--	--	-0.88**	(-1.50, -0.25)
σ^2_{int}	63.35**	--	79.80***	--
$\sigma^2_{betweenWave}$	14.01**	--	19.47**	--

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σ^2_{slope}	3.12	--	6.76*	--
$\text{COV}_{\text{int, slope}}$	-4.28	--	-9.19	--
Variance	B/σ^2	CI	B/σ^2	CI
Intercept	6.30 [^]	(6.20, 6.39)	6.52 [^]	(6.41, 6.64)
Linear Slope	-0.06 ^{**}	(-0.09, -0.02)	-0.15 [^]	(-0.19, -0.12)
σ^2_{scale}	0.04 ^{**}	--	0.10 ^{**}	--
$\text{COV}_{\text{int, scale}}$	0.38	--	1.63 ^{**}	--

Note. σ^2_{int} = variance between persons in intercept of the mean; $\sigma^2_{\text{betweenWave}}$ = variance within persons between assessments waves (i.e., months); σ^2_{slope} = variance between persons in linear slope over time; $\text{COV}_{\text{int, slope}}$ = covariance of between persons random intercept and slope; σ^2_{scale} = variance between persons in intercept of the variance; $\text{COV}_{\text{int, scale}}$ = covariance of between persons random intercept for mean with random intercept for the variance; CI = 95% Confidence Interval. * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, [^] $p \leq 0.0001$.

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Supplemental Table 4. Concurrent Association of Anxiety Symptomatology with Affect and Perception (B [95% CI])

	Positive Affect		Negative Affect	
	Mean	Variance	Mean	Variance
Within-Person				
LSAS	-0.003 (-0.009, 0.002)	-0.0002 (-0.003, 0.003)	0.003 (-0.0001, 0.007) +	0.007 (0.003, 0.010) ***
SPS	-0.009 (-0.019, 0.002)	0.003 (-0.003, 0.009)	0.014 (-0.008, 0.020) ^	0.030 (0.024, 0.036) ^
SIAS	-0.012 (-0.023, -0.001) *	0.004 (-0.002, 0.010)	0.012 (0.005, 0.019) ***	0.025 (0.019, 0.032) ^
Between-Person				
LSAS	-0.004 (-0.018, 0.011)	0.001 (-0.008, 0.010)	0.010 (0.004, 0.017) **	0.020 (0.007, 0.034) **
SPS	0.007 (-0.015, 0.029)	0.008 (-0.005, 0.021)	0.018 (0.008, 0.028) **	0.037 (0.016, 0.058) ***
SIAS	-0.009 (-0.035, 0.017)	0.001 (-0.015, 0.017)	0.019 (0.007, 0.031) **	0.041 (0.017, 0.065) ***
	Perception of Warmth		Perception of Dominance	
	Mean	Variance	Mean	Variance
Within-Person				
LSAS	-0.004 (-0.013, 0.004)	0.008 (0.004, 0.011) ^	-0.004 (-0.010, 0.002)	0.003 (-0.001, 0.006)
SPS	-0.017 (-0.032, -0.001) *	0.010 (0.004, 0.015) **	-0.004 (-0.014, 0.006)	0.002 (-0.004, 0.008)
SIAS	-0.021 (-0.037, -0.005) *	0.013 (0.007, 0.020) ***	-0.007 (-0.018, 0.003)	0.005 (-0.001, 0.012)
Between-Person				
LSAS	-0.004 (-0.019, 0.011)	0.006 (-0.003, 0.016)	-0.003 (-0.015, 0.009)	0.004 (-0.005, 0.013)
SPS	-0.018 (-0.040, 0.004)	0.016 (0.002, 0.029) *	-0.009 (-0.027, 0.010)	0.007 (-0.006, 0.021)
SIAS	-0.021 (-0.046, -0.005)	0.011 (-0.005, 0.028)	-0.004 (-0.026, 0.017)	-0.002 (-0.019, 0.014)

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Note. LSAS = Liebowitz Social Anxiety Scale; SPS = Social Phobia; SIAS = Social Interaction and Anxiety Scale; MADRS = Montgomery-Åsberg Depression Rating Scale; CI = 95% Confidence Interval. + $p \leq 0.06$, * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, ^ $p \leq 0.0001$.

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Supplemental Table 5. Concurrent Association of Anxiety Symptomatology with Interpersonal Behavior (*B* [95% CI])

	Agreeable Behavior		Quarrelsome Behavior	
	Mean	Variance	Mean	Variance
<u>Within-Person</u>				
LSAS	-0.049 (-0.117, 0.019)	-0.001 (-0.004, 0.002)	0.034 (-0.013, 0.082)	0.002 (-0.001, 0.005)
SPS	-0.086 (-0.216, 0.043)	0.002 (-0.004, 0.007)	0.076 (-0.016, 0.169)	0.004 (-0.001, 0.009)
SIAS	-0.136 (-0.273, 0.001) *	-0.0004 (-0.006, 0.005)	0.108 (0.009, 0.206) *	0.007 (0.001, 0.012) *
<u>Between-Person</u>				
LSAS	-0.081 (-0.192, 0.029)	0.002 (-0.002, 0.005)	0.004 (-0.105, 0.113)	0.001 (-0.007, 0.008)
SPS	-0.117 (-0.281, 0.047)	0.005 (-0.0003, 0.010)	0.083 (-0.079, 0.244)	0.007 (-0.004, 0.017)
SIAS	-0.109 (-0.304, 0.086)	0.005 (-0.002, 0.011)	0.051 (-0.140, 0.241)	0.011 (-0.001, 0.024)
	Dominant Behavior		Submissive Behavior	
	Mean	Variance	Mean	Variance
<u>Within-Person</u>				
LSAS	-0.128 (-0.191, -0.066) ***	-0.002 (-0.005, 0.001)	0.156 (-0.076, 0.237) ***	0.006 (0.002, 0.009) ***
SPS	-0.230 (-0.344, -0.115) ***	0.001 (-0.004, 0.006)	0.270 (0.120, 0.421) ***	0.006 (0.0001, 0.011) *
SIAS	-0.239 (-0.361, -0.117) ***	0.002 (-0.003, 0.008)	0.260 (0.100, 0.419) **	0.009 (0.003, 0.014) **
<u>Between-Person</u>				
LSAS	-0.207 (-0.312, -0.101) ***	-0.001 (-0.004, 0.003)	0.252 (-0.142, 0.362) ^	0.006 (0.001, 0.011) *
SPS	-0.313 (-0.485, -0.142) ***	0.001 (-0.005, 0.007)	0.316 (0.139, 0.493) ***	0.005 (-0.003, 0.013)

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SIAS -0.281 (-0.481, -0.081) ** 0.001 (-0.006, 0.008) 0.320 (0.104, 0.535) ** 0.009 (0.0003, 0.018) *

Note. LSAS = Liebowitz Social Anxiety Scale; SPS = Social Phobia; SIAS = Social Interaction and Anxiety Scale; MADRS = Montgomery-Åsberg Depression Rating Scale; CI = 95% Confidence Interval. * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, ^ $p \leq 0.0001$.