

## Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work

## **eAppendix 1. Methods**

**FreeSurfer Method Details:** Two 3D T1-weighted magnetization prepared rapid gradient echo (MPRAGE) scans were acquired sagittally (TR 2,300ms, TE 3.16ms, TI 1,200ms, flip angle 8°, 160 slices, 256 × 256 matrix, field of view 256mm, 1.0-mm<sup>3</sup> voxels, 6:18 min per scan). The white and pial surfaces generated by FreeSurfer were visually inspected, and when necessary appropriate edits were performed and the surfaces regenerated. For approximately 10% of scans, poor scan quality required discarding them from further analysis (N = 29, 22, and 18 at the three waves, respectively). In those cases, all data were generated from within-subject templates using the remaining scans. Cortical gray matter volume for the left and right hemispheres was obtained from the “CortexVol” measures in FreeSurfer’s “aseg.stats” report. Surface area (of the white matter surface) and cortical thickness for the left and right hemispheres were obtained from the “WhiteSurfArea” and “MeanThickness” summary measures in the “aparc.stats” report for each hemisphere. Volumes and surface area were summed across hemispheres, and thickness averaged across hemispheres to obtain the respective “global” measures.

## **eAppendix 2. Results**

### **The P-SA-MDD and MDD Diagnosis Comparisons:**

The P-SA-MDD score significantly differentiated depressed from non-depressed groups in numerous ways both for preschool and school age MDD as well as for those who experience MDD any time prior to and including scan 1 ( $p < 0.0001$  for all comparisons). It was also correlated with the proportion of waves with a depressive episodes prior to and including scan 1 (0.83,  $p < 0.0001$ ).

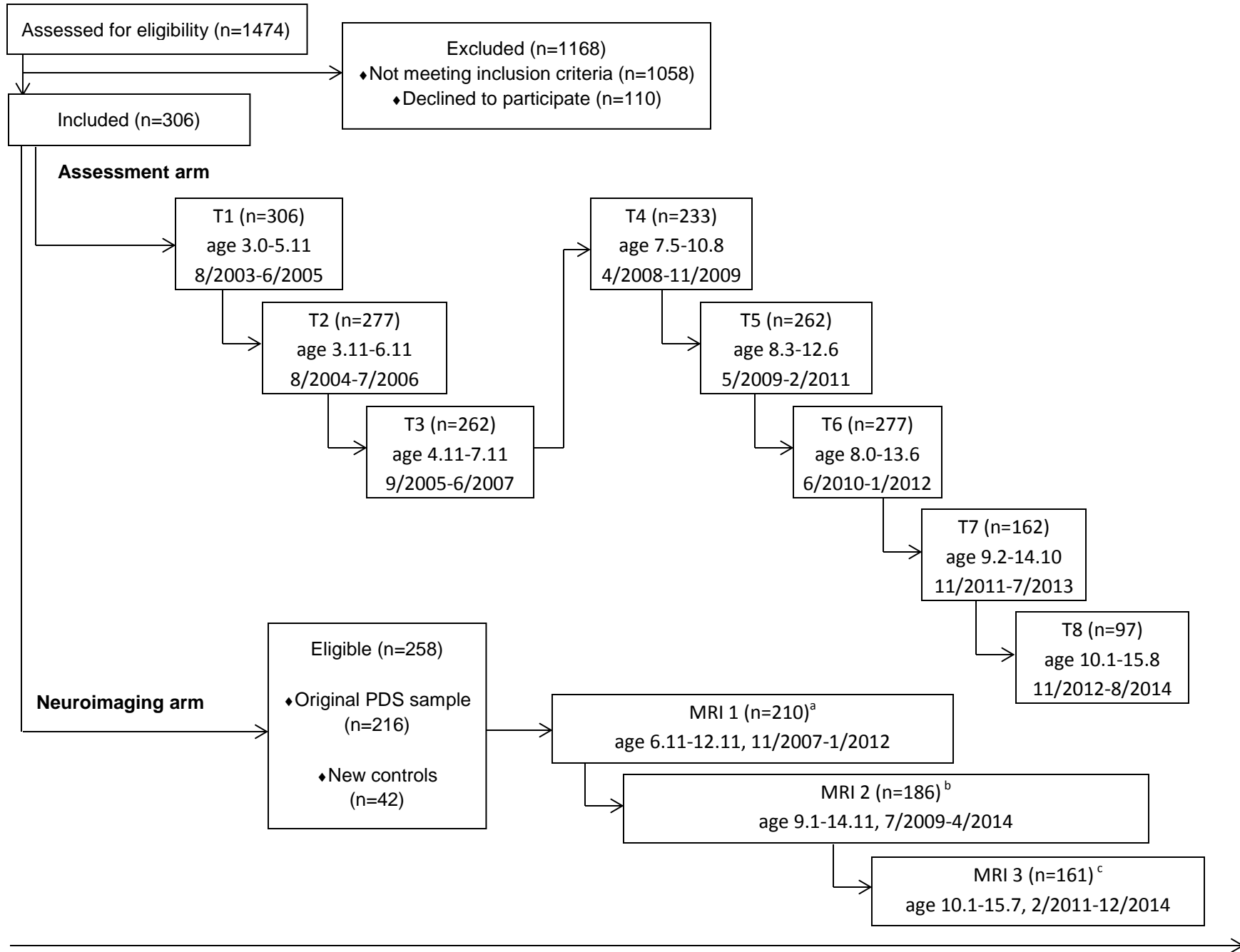
**MLM Models with Medicated Subjects Removed:** A trend level interaction of P-SA-MDD severity with time for global cortical gray volume ( $B = -1.04$ ,  $SE = 0.56$ ,  $t = -1.84$ ,  $p = 0.0684$ ) and a significant severity by time interaction for global cortical gray thickness ( $B = -0.0046$ ,  $SE = 0.0021$ ,  $t = -2.15$ ,  $p = 0.0338$ ) indicated greater declines for those with high levels of P-SA-MDD severity.

**MLM Models with Parent CDI scores:** In the models using mean parent-reported CDI total T-score, the interaction was not significant for volume ( $B = -0.10$ ,  $SE = 0.08$ ,  $t = -1.21$ ,  $p = 0.2273$ ), thickness ( $B = -0.0004$ ,  $SE = 0.0003$ ,  $t = -1.41$ ,  $p = 0.1591$ ), or surface area ( $B = -0.01$ ,  $SE = 0.10$ ,  $t = -0.11$ ,  $p = 0.9128$ ), however coefficient estimates are trending in the same direction as those using child-reported CDI).

### **Brain Regions Examined:**

Volume, thickness, and surface area of the insula, anterior cingulate gyrus and sulcus, middle anterior cingulate gyrus and sulcus, inferior frontal sulcus, subcallosal gyrus, straight gyrus, middle frontal gyrus, middle occipital gyrus, occipital pole, cuneus, superior frontal gyrus, inferior frontal gyrus, orbital gyrus, and superior temporal cortex were investigated. In addition, amygdala, hippocampus, thalamus, caudate, putamen, nucleus accumbens, and pallidum volumes were examined.

**eFigure 1.** Flow of the PDS Study



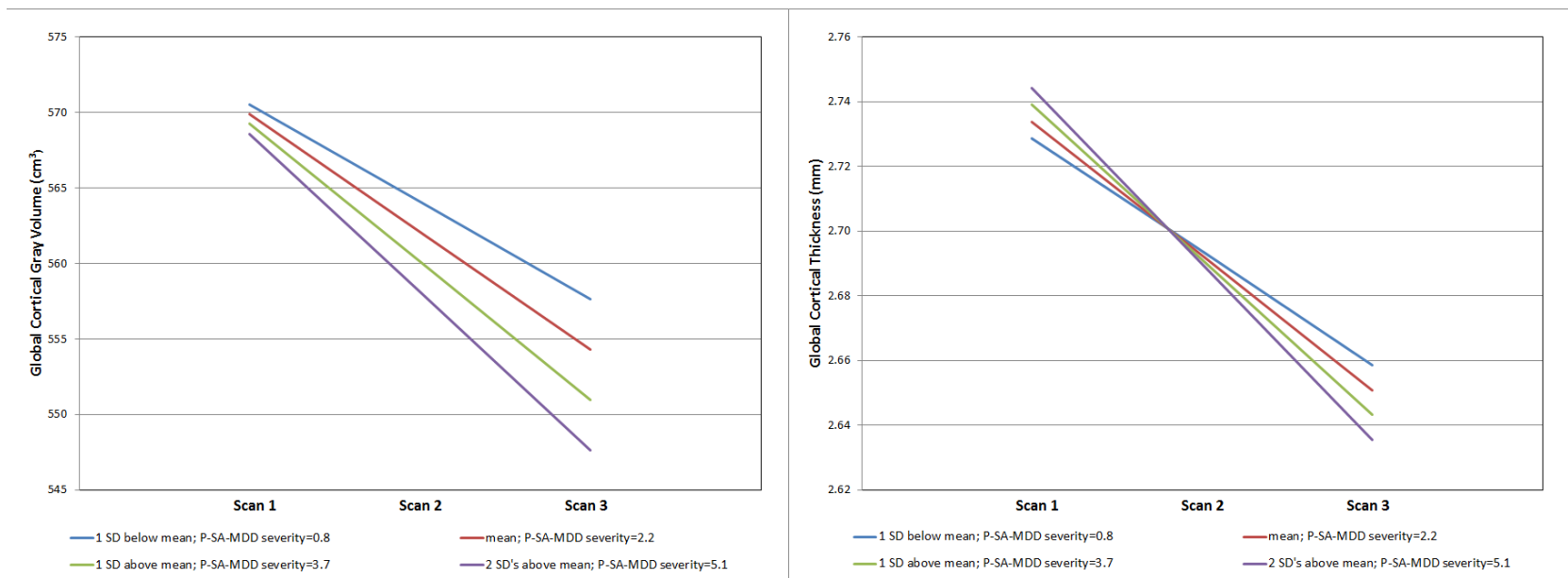
<sup>a</sup> N=210 subjects had a Scan 1, but N=29 subjects had unusable scan data and N=7 did not have IQ data, so Scan 1 data was included in analyses for N=174 subjects. N=1 subject did not have their first scan in time for it to be considered a Scan 1.

<sup>b</sup> Of N=211 potential Scan 2 subjects, N=22 subjects had unusable scan data, N=3 did not have IQ data, N=18 refused participation, and N=7 had braces, so Scan 2 data was included in analyses for N=161 subjects.

<sup>c</sup> Of N=211 potential Scan 3 subjects, N=18 subjects had unusable scan data, N=3 did not have IQ data, N=20 refused participation, N=14 had braces, and N=16 had too little time elapsed after Scan 2, so Scan 3 data was included in analyses for N=140 subjects.

Exclusion criteria included (i) contraindications for MRI scanning; (ii) head injury with loss of consciousness >5 min; (iii) neurological illness; (iv) diagnosis of a pervasive developmental disorder; and (v) treatment for lead poisoning.

**eFigure 2.** Estimated Trajectories of Global Cortical Gray Volume and Global Cortical Thickness by P-SA-MDD Severity in 193 Subjects



**eTable 1.** Stressful and Traumatic Life Events

<b>Stressful Life Events</b>
Break up with best friend
Break up with boyfriend or girlfriend
Change in daycare or school
Death of a pet
Forced separation from home
Lives or attends school in an unsafe environment
Loss of home without family separation
Loss of significant person through moving
Marital family conflict
Moving house
New child in home
New parental figure
Parental arrest
Parental divorce
Parental hospitalization
Parental separation
Reduction in standard of living
Separation from parent (1 week or more)
<b>Traumatic Life Events</b>
Accident or crash with automobile, plane, or boat
Accidental burning, poisoning, or drowning
Attacked by an animal
Event causing death or severe harm
Death of adult loved one
Death of sibling or peer
Diagnosis of physical illness
Domestic violence
Held in captivity
Hospitalization, emergency room visit, or invasive medical procedure
Impregnated someone
Learned about a traumatic event
Learned about exposure to noxious agent
Man-made disaster (fire, war, terrorism)
Natural disaster (flood, hurricane, tornado, earthquake)
Physical abuse
Pregnancy
Sexual abuse, sexual assault, or rape
Victim of physical violence
Witnessed someone threatened with harm, seriously injured, or killed
Other traumatic life event

**eTable 2.** Multilevel Mixed Models of Left and Right Global Cortical Gray Volume and Global Cortical Thickness in 193 Subjects

<b>Left Global Cortical Gray Volume</b>	<b>Estimate (cm<sup>3</sup>)</b>	<b>SE</b>	<b>t</b>	<b>P</b>
Intercept	277.47	2.90	95.60	<0.0001
Age	-1.44	1.31	-1.10	0.2731
Age squared	1.10	0.86	1.28	0.2032
Gender (male=1, female=0)	22.21	3.35	6.63	<0.0001
Income to needs	4.25	1.90	2.24	0.0260
IQ score	0.48	0.12	3.95	0.0001
Time <sup>a</sup>	-4.03	0.31	-12.90	<0.0001
P-SA-MDD severity	0.36	1.30	0.28	0.7821
P-SA-MDD severity X Time	-0.51	0.21	-2.40	0.0175
<b>Right Global Cortical Gray Volume</b>	<b>Estimate (cm<sup>3</sup>)</b>	<b>SE</b>	<b>t</b>	<b>P</b>
Intercept	277.95	2.94	94.64	<0.0001
Age	-1.30	1.33	-0.97	0.3312
Age squared	1.14	0.88	1.31	0.1933
Gender (male=1, female=0)	22.34	3.41	6.56	<0.0001
Income to needs	4.04	1.93	2.09	0.0376
IQ score	0.48	0.12	3.83	0.0002
Time	-3.76	0.31	-12.15	<0.0001
P-SA-MDD severity	0.12	1.31	0.09	0.9289
P-SA-MDD severity X Time	-0.41	0.21	-1.95	0.0530
<b>Left Global Cortical Thickness</b>	<b>Estimate (mm)</b>	<b>SE</b>	<b>t</b>	<b>P</b>
Intercept	2.7787	0.0117	237.74	<0.0001
Age	-0.0284	0.0049	-5.84	<0.0001
Age squared	-0.0006	0.0032	-0.18	0.8545
Gender (male=1, female=0)	0.0127	0.0124	1.02	0.3085
Income to needs	0.0047	0.0070	0.67	0.5041
IQ score	0.0006	0.0005	1.22	0.2237
Time	-0.0433	0.0025	-17.19	<0.0001
P-SA-MDD severity	0.0089	0.0056	1.58	0.1157
P-SA-MDD severity X Time	-0.0050	0.0017	-2.94	0.0038
<b>Right Global Cortical Thickness</b>	<b>Estimate (mm)</b>	<b>SE</b>	<b>t</b>	<b>P</b>
Intercept	2.7591	0.0113	243.33	<0.0001
Age	-0.0256	0.0047	-5.40	<0.0001
Age squared	0.0014	0.0031	0.45	0.6525
Gender (male=1, female=0)	0.0136	0.0121	1.12	0.2647
Income to needs	0.0050	0.0069	0.73	0.4693
IQ score	0.0006	0.0004	1.43	0.1531
Time	-0.0397	0.0024	-16.33	<0.0001
P-SA-MDD severity	0.0071	0.0054	1.30	0.1943
P-SA-MDD severity X Time	-0.0039	0.0016	-2.34	0.0204



<sup>a</sup> Defined as scan number

**eTable 3.** Multilevel Mixed Models of Global Cortical Gray Volume Separately by Sex

<b>Male Subjects (N=99)</b>	<b>Estimate (cm<sup>3</sup>)</b>	<b>SE</b>	<b>t</b>	<b>p</b>
Intercept	595.68	7.06	84.38	<0.0001
Age	-0.28	4.26	-0.07	0.9476
Age squared	2.16	2.60	0.83	0.4083
Income to needs	7.02	5.74	1.22	0.2242
IQ score	1.06	0.39	2.74	0.0074
Time <sup>a</sup>	-5.96	0.82	-7.26	<0.0001
P-SA-MDD severity	-0.79	4.00	-0.20	0.8445
P-SA-MDD severity X Time	-1.05	0.54	-1.95	0.0547
<b>Female Subjects (N=94)</b>	<b>Estimate (cm<sup>3</sup>)</b>	<b>SE</b>	<b>t</b>	<b>p</b>
Intercept	561.02	6.10	91.93	<0.0001
Age	-4.67	3.29	-1.42	0.1596
Age squared	1.60	2.39	0.67	0.5047
Income to needs	9.53	5.10	1.87	0.0646
IQ score	0.88	0.31	2.81	0.0061
Time	-9.61	0.89	-10.75	<0.0001
P-SA-MDD severity	2.50	3.33	0.75	0.4537
P-SA-MDD severity X Time	-1.15	0.63	-1.82	0.0737

<sup>a</sup> Defined as scan number

**eTable 4.** Multilevel Mixed Models of Global Cortical Gray Thickness Separately by Sex

<b>Male Subjects (N=99)</b>	<b>Estimate (mm)</b>	<b>SE</b>	<b>t</b>	<b>p</b>
Intercept	2.7729	0.0128	216.77	<0.0001
Age	-0.0296	0.0065	-4.52	<0.0001
Age squared	-0.0004	0.0040	-0.09	0.9289
Income to needs	-0.0025	0.0088	-0.29	0.7731
IQ score	0.0004	0.0006	0.74	0.4591
Time <sup>a</sup>	-0.0355	0.0035	-10.26	<0.0001
P-SA-MDD severity	0.0018	0.0075	0.24	0.8143
P-SA-MDD severity X Time	-0.0056	0.0023	-2.49	0.0151
<b>Female Subjects (N=94)</b>	<b>Estimate (mm)</b>	<b>SE</b>	<b>t</b>	<b>p</b>
Intercept	2.7794	0.0143	194.95	<0.0001
Age	-0.0234	0.0071	-3.31	0.0014
Age squared	0.0025	0.0052	0.49	0.6253
Income to needs	0.0112	0.0110	1.02	0.3101
IQ score	0.0008	0.0007	1.12	0.2638
Time	-0.0471	0.0033	-14.27	<0.0001
P-SA-MDD severity	0.0171	0.0081	2.12	0.0371
P-SA-MDD severity X Time	-0.0041	0.0023	-1.76	0.0825

<sup>a</sup> Defined as scan number

**eTable 5.** Effect Size of P-SA-MDD Severity in Multilevel Mixed Models in 193 Subjects

<b>Brain Region</b>	<b>Effect size<sup>a</sup></b>
Global cortical volume	-0.156
Insula volume	-0.001
Anterior cingulate gyrus and sulcus volume	-0.047
Middle anterior cingulate gyrus and sulcus volume	-0.102
Inferior frontal sulcus volume	-0.081
Subcallosal gyrus volume	-0.112
Straight gyrus volume	-0.133
Middle frontal gyrus volume	-0.055
Middle occipital gyrus volume	-0.051
Occipital pole volume	0.022
Cuneus volume	0.006
Superior frontal gyrus volume	-0.139
Inferior frontal gyrus volume	-0.121
Orbital gyrus volume	-0.123
Superior temporal cortex volume	-0.134
Amygdala volume	0.007
Hippocampus volume	-0.050
Thalamus volume	-0.078
Caudate volume	0.002
Putamen volume	0.028
Nucleus accumbens volume	0.050
Pallidum volume	0.046
Global cortical thickness	-0.189
Insula thickness	-0.078
Anterior cingulate gyrus and sulcus thickness	-0.105
Middle anterior cingulate gyrus and sulcus thickness	-0.114
Inferior frontal sulcus thickness	-0.111
Subcallosal gyrus thickness	-0.085
Straight gyrus thickness	-0.068
Middle frontal gyrus thickness	-0.140
Middle occipital gyrus thickness	-0.140
Occipital pole thickness	0.024
Cuneus thickness	-0.027
Superior frontal gyrus thickness	-0.154
Inferior frontal gyrus thickness	-0.143
Orbital gyrus thickness	-0.134
Superior temporal cortex thickness	-0.131

<b>Brain Region</b>	<b>Effect size<sup>a</sup></b>
Global cortical surface area	-0.067
Insula surface area	0.030
Anterior cingulate gyrus and sulcus surface area	-0.101
Middle anterior cingulate gyrus and sulcus surface area	-0.017
Inferior frontal sulcus surface area	-0.100
Subcallosal gyrus surface area	-0.041
Straight gyrus surface area	-0.122
Middle frontal gyrus surface area	0.033
Middle occipital gyrus surface area	0.101
Occipital pole surface area	0.019
Cuneus surface area	-0.050
Superior frontal gyrus surface area	-0.051
Inferior frontal gyrus surface area	-0.079
Orbital gyrus surface area	-0.044
Superior temporal cortex surface area	-0.176

<sup>a</sup> Effect sizes are correlations between P-SA-MDD severity and subjects' individual slope estimates from the multilevel model