Supplementary Online Content

Pierce LJ, Thompson BL, Gharib A, et al. Association of perceived maternal stress during the perinatal period with electroencephalography patterns in 2-month-old infants. *JAMA Pediatr*. Published online April 8, 2019. doi:10.1001/jamapediatrics.2019.0492

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

eTable 1. Comparison of infants retained versus excluded from EEG analysis

	Retained	Excluded		
	Mean (SD) **N**	**Mean(SD)** **n**	**95% CI**	***p***
Child age (months)	2.42(.37) 70	2.32 (.26) 43	-.22, .03	0.14
Maternal age (years)	29.2 (5.69) 70	27.72 (5.34) 43	-3.62, .66	0.17
Child weight at birth (grams)	3356.34 (485.33) 69[a]	3211.60 (431.99) 41[a]	-326.99, 37.52	0.12
Maternal education				
Less than high school	0.23(.42)	0.16(.37)	.319, 1.59	0.40
High school	0.50(.50)	0.44(.50)	.587, 1.33	0.55
Associate's or higher	0.24(.43) 68[b]	0.37(.49) 42[b]	.869, 2.70	0.15
% Families in neighborhood below poverty line	24.6(11.2) 69[b]	22.2 (7.6) 41[b]	-.06, .02	0.23
Perceived Stress Scale	11.13(7.36) 53[c]	11.74 (6.78) 27[b (3),c (13)]	-2.77, 3.98	0.72
Recent Life Events	1.5 (1.62) 70	1.15 (1.46) 41[b]	-.96, .24	0.25

[a]data not available, [b]did not wish to disclose, [c]not administered

eTable 2. Comparison of absolute and relative EEG power across sites

	BCH	CHLA		
	Mean(SD)	**Mean(SD)**	**95% CI**	***p***
Log_{10} transformed absolute EEG power				
Delta	-.229(.223)	-.209(.201)	-.12, .08	0.70
Theta	-.635(.233)	-.574(.209)	-.17, .04	0.25
Low Alpha	-.461(.208)	-.445(.173)	-.11, .08	0.72
High Alpha	-.324(.198)	-.347(.163)	-.06, .11	0.59
Beta	.101(.186)	.033(.162)	-.02, .15	0.11
Gamma	-.003(.191)	-.080(.172)	-.01, .16	0.08
Relative EEG power				
Delta	.152(.024)	.172(.028)	-.03, -.01	0.003
Theta	.060(.011)	.074(.012)	-.02, -.01	<0.001
Low Alpha	.089(.010)	.099(.011)	-.02, -.01	<0.001
High Alpha	.121(.012)	.124(.010)	-.01, .003	0.33
Beta	.322(.023)	.299(.024)	.01, .03	<0.001
Gamma	.256(.032)	.232(.027)	.01, .04	0.001

eTable 3. Regression to determine whether variables of interest vary as a function of site for EEG profile membership

	Probability of Membership in Low Relative EEG Profile	
	Unstandardized Estimate (b)	**95% CI**
Infant Age	1.01	-2.03,4.05
Site	-2.25	-3.43,-1.07
Site X Age	0.31	-4.04,4.66
Perceived Stress	0.01	-0.15,0.17
Site	-2.34	-3.61,-1.07
Perceived Stress X Site	-0.049	-.106,.286

CI = Confidence Intervals

eTable 4. Regression to determine whether variables of interest vary as a function of site for individual frequency bands[a]

	Delta	Theta	Low Alpha	Beta	Gamma
	B [95% CI]	B [95% CI]	B [95% CI]	B [95% CI]	B [95% CI]
Infant Age	.021⁺ [-.001,.044]	.013** [.004,.023]	-.004 [-.013,.005]	-.020+ [-.039,.000]	-.003 [-.029,.022]
Site	-.016* [-.029,-.004]	-.012*** [-.018,-.006]	-.010*** [-.015,-.005]	.019** [.008,.030]	.022** [.007,.036]
Site X Age	-.010 [-.046,.027]	-.006 [-.023,.010]	.013⁺ [-.002,.028]	-.002 [-.035,.030]	-.018 [-.060,.023]

[a]Regressions conducted for frequency bands that show significant differences in relative power between sites

$^{+}p < 0.10$; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$

eTable 5. Correlations between demographic variables[a]

	1	2	3	4	5	6	7	8	9	10	11
1. Site[b]	-										
2. Infant Age (months)	.27*	-									
3. Maternal Age (years)	-.01	-.06	-								
4. Infant birth weight (grams)	.09	.17	.18	-							
5. Family Income	-.63***	-.21	.34*	-.02	-						
6. Neighborhood Poverty (%)	.48***	.28*	-.19	.14	-.59***	-					
7. Maternal Education (< highschool)	.34**	.11	-.10	-.03	-.30*	.23⁺	-				
8. Maternal Education (highschool)	.09	.03	-.27*	-.05	-.18	.10	-.54***	-			
9. Maternal Education (College +)	-.37**	-.11	.42***	.05	.46***	-.36**	-.31**	-.57***	-		
10. Number Reported Recent Life Events	-.10	.08	-.21⁺	-.06	-.28*	.09	-.19	.17	-.09	-	
11. Perceived Stress Score	.10	-.08	-.24⁺	-.11	-.18	.04	-.07	.26⁺	-.20	.40**	-

[a]Pearson *r*, two-tailed; [b]BCH = 0, CHLA = 1
⁺ $p < 0.10$; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

eTable 6. Regression of log10 transformed absolute infant EEG power on maternal sensitivity residual scores

	Delta	**Theta**	**Low Alpha**	**High Alpha**	**Beta**	**Gamma**
	B [95% CI] r_{sp}	B [95% CI] r_{sp}	B [95% CI] r_{sp}	B [95% CI] r_{sp}	B [95% CI] r_{sp}	B [95% CI] r_{sp}
Step 2						
Infant Age	.271*** [.145,.396] .445	.300*** [.170,.431] .470	.222*** [.106,.337] .405	.217*** [.110,.325] .418	.160** [.056,.264] .314	.157** [.050,.265] .296
Neighborhood Poverty (%)	-.138 [-.576,.301] -.065	.003 [-.454,.460] .001	-.054 [-.458,.350] -.028	-.175 [-.551,.200] -.096	-.074 [-.438,.290] -.042	.015 [-.362,.392] .008
Maternal Education						
High School	.095+ [-.012,.202] .184	.066 [-.045,.177] .122	.069 [-.029,.168] .149	.082+ [-.009,.173] .185	.095* [.006,.184] .220	.112* [.019,.205] .248
College +	.126+ [-.007,.259] .195	.128+ [-.010,.267] .189	.125* [.002,.247] .214	.134* [.020,.248] .243	.169** [.057,.280] .312	.184** [.068,.299] .325
Maternal Sensitivity	-.035 [-.086,.016] -.159	-.032 [-.085,.020] -.139	-.033 [-.078,.013] -.164	-.029 [-.071,014] -.152	-.046* [-.087,-.006] -.251	-.055* [-.097,-.013] -.284
R^2 Change	.027	.021	.028	.024	.064*	.082*

+$p < 0.10$; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

eTable 7. Regression of relative infant EEG power on maternal sensitivity residual scores

	Delta	Theta	Low Alpha	High Alpha	Beta	Gamma
	B [95% CI] r_{sp}	B [95% CI] r_{sp}	B [95% CI] r_{sp}	B [95% CI] r_{sp}	B [95% CI] r_{sp}	B [95% CI] r_{sp}
Step 2						
Infant Age	.025** [.007.044] .312	.015** [.006,.023] .368	.004 [-.004,.012] .124	.005 [-.002,.013] .163	-.027** [-.044,-.010] -.356	-.022* [-.044, -.001] -.246
Neighborhood Poverty (%)	-.022 [-.086,.043] -.076	.012 [-.019,.042] .083	.002 [-.026,.030] .017	-.035* [-.061,-.008] -.301	-.004 [-.063,.054] -.016	.047 [-.028,.122] .147
Maternal Education						
High School	.001 [-.014,.017] .019	-.004 [-.011,.004] -.108	-.005 [-.011,.002] -.163	-.003 [-.009,.004] -.095	.001 [-.013,.016] .020	.008 [-.010,.026] .108
College +	-.010 [-.014,.017] .019	-.004 [-.013,.006] -.086	-.006 [-.015,.002] -.171	-.006 [-.014,.002] -.165	.010 [-.008,.028] .124	.016 [-.007,.038] .163
Maternal Sensitivity	.002 [-.006,.010] .067	.001 [-.002,.005] .090	.001 [-.002.005] .121	.003 [-.001,006] .229	-.003 [-.010,-.004] -.106	-.005 [-.014,-.005] -.138
R^2 Change	.010	.011	.019	.057^{+}	.014	.023

$^{+}p < 0.10$; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$

eTable 8. Regression of infant EEG profiles on maternal sensitivity residual scores: latent profile analysis

	Probability of Membership in Low Relative EEG Profile		
	Unstandardized Estimate (b)	**95% CI**	**AOR**
Infant Age	2.7	.583,4.82	14.88
Maternal Education High School	-.70	-2.25,.848	.50
College+	-.46	-2.28,1.36	.63
% Neighbourhood Poverty	-.60	-5.97,4.77	.55
Maternal Sensitivity	1.07	.208,1.93	2.92

CI = Confidence Interval; AOR = Adjusted Odds Ratio

eTable 9. Tests of sex effects in log10 transformed absolute infant EEG power for maternal perceived stress scores

	Beta	Gamma
	B [95% CI] r_{sp}	B [95% CI] r_{sp}
Step 2		
Infant Age	.148** [.042,.253] .288	.147** [.037, .258] .275
Neighborhood Poverty (%)	-.051 [-.416,.314] -.028	.034 [-.348,.415] .018
Maternal Education High school	.089⁺ [-.001,.179] .203	.109* [.014,.203] .236
College +	.163** [.050,.276] .294	.182** [.064,.301] .315
Recent Life Events	.023⁺ [-.002,.048] .187	.022 [-.004,.048] .174
Perceived Stress	-.011* [-.019,-.002] -.300	-.011* [-.020,-.003] -.304
Child sex	-.060 [-.204,.084] -.091	-.062 [-.218,.094] -.090
Perceived Stress X Sex	.008 [-.003,.019] .165	.007 [-.005,.018] .133

[a]Regressions conducted for frequency bands that show significant differences in log10 transformed absolute power
$^{+}p < 0.10$; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$

eTable 10. Tests of sex effects in log10 transformed absolute infant EEG power for maternal sensitivity residual scores[a]

	Beta	Gamma
	B [95% CI] r_{sp}	B [95% CI] r_{sp}
Step 2		
Infant Age	.149** [.043,.255] .291	.147** [.037, .258] .275
Neighborhood Poverty (%)	-.048 [-.412,.316] -.027	.036 [-.342,.414] .019
Maternal Education High school	.094* [.005,.182] .216	.111* [.019,.204] .246
College +	.158** [.045,.271] .286	.177** [.059,.296] .308
Maternal Sensitivity	-.076* [-.137,-.015] -.291	-.083* [-.147,-.018] -.303
Child sex	.027 [-.048,.101] .073	.012 [-.066,.090] .031
Maternal Sensitivity X Sex	.057 [-.023,.137] .157	.053 [-.034,.140] .141

[a]Regressions conducted for frequency bands that show significant stress effects in log10 transformed absolute power
$^{+}p < 0.10$; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$

eTable 11. Tests of sex effects in latent profile analysis of relative EEG profiles for maternal perceived stress[a]

	Probability of Membership in Low Relative EEG Profile		
	Unstandardized Estimate (b)	**95% CI**	**AOR**
Infant Age	2.5	.364,4.64	12.18
Maternal Education High School	-.63	-2.28,1.02	.53
College +	-.67	-2.41,1.07	.51
% Neighbourhood Poverty	-.66	-6.01,4.69	.52
Recent Life Events	-.25	-.720,.220	.78
Perceived Stress	.15	.013,.287	1.16
Sex	.72	-1.93,3.37	2.05
Perceived Stress X Sex	-.05	-.246,.146	.95

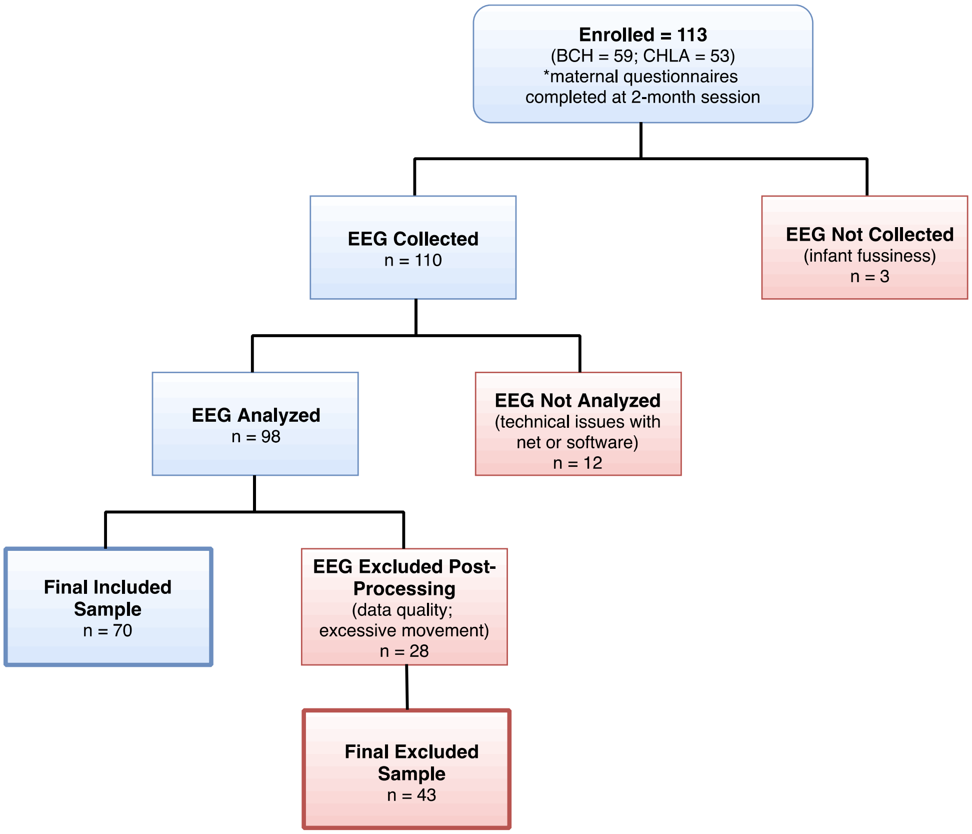
[a]Regressions conducted for profile that shows significant stress effects
CI = Confidence Intervals; AOR = Adjusted Odds Ratio

eTable 12. Tests of sex effects in latent profile analysis of relative EEG profiles for maternal sensitivity residual scores[a]

	Probability of Membership in Low Relative EEG Profile		
	Unstandardized Estimate (b)	**95% CI**	**AOR**
Infant Age	2.85	.576,5.12	17.29
Maternal Education High School	-.77	-2.46,.916	.46
College +	-.50	-2.32,1.32	.60
% Neighbourhood Poverty	-.70	-6.30,4.91	.50
Maternal Sensitivity	1.26	.201,2.32	3.52
Sex	.22	-1.03,1.47	1.24
Maternal Sensitivity X Sex	-.38	-1.83,1.07	.68

[a]Regressions conducted for profile that shows significant stress effects
CI = Confidence Intervals; AOR = Adjusted Odds Ratio

eFigure. Flowchart indicating participant exclusions



*See eTable1 for questionnaire exclusions in included and excluded samples

eMethods. Supplementary methods

EEG Analysis – HAPPE Processing Pipeline

Within HAPPE, data were band-pass filtered at 1-249 Hz. To optimize performance of independent component analysis (ICA) for artifact rejection a subset of 46 channels was selected for further processing. The number of selected channels was based on recording length[1] and channel locations included standard 10-20 (9, 11, 22, 24, 33, 36, 45, 52, 58, 62, 70, 83, 92, 96, 104, 108, 122, 124) and additional electrodes representative of specific regions across the cerebral hemispheres based on previous infant reports, including those with infants from low SES backgrounds (3, 4, 13, 19, 20, 23, 27, 28, 40, 41, 46, 47, 66, 67, 71, 72, 75, 76, 77, 84, 98, 102, 103, 109, 112, 117, 118, 123)[2,3]. A multi-taper regression approach using CleanLine[4] was used to remove 60 Hz electrical line-noise. Channels with poor signal quality were identified using joint probability evaluation and interpolated using spherical interpolation following ICA decomposition. Wavelet-enhanced ICA (W-ICA) was performed using the extended Infomax algorithm and a Coiflets (level 5) wavelet to remove large EEG artifacts such as high amplitude eye and motor movements.[5] Wavelet thresholding attenuates the EEG signal resulting in lower overall amplitudes however this does not impact analysis and interpretation and significantly improves subsequent ICA decomposition. Following W-ICA, ICA decomposition with automatic component rejection was performed using the Multiple Artifact Rejection Algorithm (MARA)[6,7] to correct any remaining artifacts, including artifact from muscle movements not typically detected via other algorithms but which can be prominent in infant EEG data. Components with artifact probabilities greater than 0.5 compared to neural signal were rejected. Data were segmented into 2-second segments, and segments with remaining artifact were removed via amplitude-based (+/-40 uV) criteria. Data were re-referenced to the average of all channels.

EEG Analysis – Data Exclusion Criteria

EEG data were excluded from subsequent analysis if < 20 2-second segments were available (M_{retained} = 131; *SD* = 11.53; range = 77 – 145), if > 9 channels were interpolated (*M* = 5.0, *SD* = 2.27, range = 0 – 9), if the percentage of independent components (ICs) rejected was > 70% (M_{ICs} rejected = 47.4%, *SD* = 10.3%, range = 28.9% – 69.8%), and if the mean (*M* = 0.24, *SD* = 0.03, range = 0.17 – 0.30) and median (*M* = 0.23, *SD* = 0.05, range = 0.13 – 0.30) probabilities of artifact present in remaining ICs was > 0.3. Probability of artifact in ICs was calculated prior to subsequent artifact rejection and therefore overestimates the amount of artifact remaining in the data. This statistic is used to determine data quality for exclusion of high-artifact data from subsequent processing, not actual artifact present in the processed EEG signal[1].

Site Differences in Absolute and Relative EEG Power

Because EEG was acquired using different amplifier models at BCH and CHLA independent samples t-tests were conducted to compare EEG power in each frequency band across sites. No significant site differences were observed in any frequency band for absolute EEG power (all $p > 0.10$), however infants at CHLA had significantly higher relative delta, theta, and low alpha power and significantly lower relative beta and gamma power than BCH (eTable2). Because site is highly correlated with key variables of interest (infant age, poverty, maternal education), including site as a covariate in statistical models will result in high levels of shared variance that is likely to reduce effects. To ensure effects of interest in relative power were not due solely to unanticipated site differences, we regressed variable by site interaction terms for variables showing significant main effects (i.e., infant age, maternal PSS scores) on relative EEG outcomes (relative EEG profile membership; relative power in individual frequency bands). Associations did not vary as a function of site (eTable3; eTable4), and thus we collapsed across sites for all analyses.

Multinomial Linear Regression in MPlus

The 3-Step method (deployed in MPlus) is a robust procedure for identifying latent profiles using LPA and subsequently testing associations between variables of interest and profile membership.[8] In step 1 the latent class model is estimated. In step 2, a "most likely class" variable is created using the latent class posterior distribution obtained in step 1. In step 3, this most likely class variable is used as a nominal latent class indicator variable. The inclusion of auxiliary variables in this final step allows identified profiles to be regressed onto variables of interest using multinomial logistic regression.

eReferences

1. Gabard-Durnam LJ, Mendez Leal AS, Wilkinson CL, Levin AR. The Harvard Automated Processing Pipeline for Electroencephalography (HAPPE): standardized processing software for developmental and high-artifact data. *Front Neurosci*. 2018;12:97.

2. Tomalski P, Moore DG, Ribeiro H, Axelsson EL, Murphy E, Karmiloff-Smith A, Johnson MH, Kushnerenko E. Socioeconomic status and functional brain development–associations in early infancy. *Dev Sci*. 2013;16(5):676-87.

3. Tierney AL, Gabard-Durnam L, Vogel-Farley V, Tager-Flusberg H, Nelson CA. Developmental trajectories of resting EEG power: an endophenotype of autism spectrum disorder. *PloS One*. 2012;7(6):e39127.

4. Mullen, T. (2012). *NITRC: CleanLine: Tool/Resource Info*. Available online at: http://www.nitrc.org/projects/cleanline.

5. Jung TP, Humphries C, Lee TW, Makeig S, McKeown MJ, Iragui V, Sejnowski TJ. Extended ICA removes artifacts from electroencephalographic recordings. In Advances in neural information processing systems 1998 (pp. 894-900).

6. Winkler I, Haufe S, Tangermann M. Automatic classification of artifactual ICA-components for artifact removal in EEG signals. *Behav Brain Funct*. 7(1):30.

7. Winkler I, Brandl S, Horn F, Waldburger E, Allefeld C, Tangermann M. Robust artifactual independent component classification for BCI practitioners. *J Neural Eng*. 2014;11(3):035013.

8. Asparouhov T, Muthén B. Auxiliary variables in mixture modeling: Using the BCH method in Mplus to estimate a distal outcome model and an arbitrary secondary model. Mplus Web Notes. 2014;21(2):1-22.