

INTRODUCTION

Maternal Anxiety:

- 8-9% of postpartum women report elevated anxiety¹
- maternal stress/anxiety is linked to:
 - infant socioemotional development^{2,3}
 - differences in child-brain morphometry⁴ Ο

Infant Temperament:

- risk for anxiety is linked to fearful temperament (e.g., negative reactivity at 4 mo., behavioral inhibition (BI) at 2 years) ^{5, 6}
- anxiety and BI have been linked to differences in brain morphometry in childhood, adolescence, and adulthood ^{7, 8, 9}

Maternal Anxiety X Infant Temperament:

• one study found that the interaction between BI and decreased hippocampal volume in adolescence was moderated by whether the individual's parent had a panic disorder diagnosis ¹⁰

However, it remains unknown whether these factors influence *infant* brain development.

RESEARCH QUESTION

Does the interaction between maternal anxiety and negative affect at 4 months predict differences in *infant* brain morphometry?

HYPOTHESIS

Greater negative affect and maternal anxiety will be associated with...

- decreased hippocampal volume
- increased amygdala volume
- decreased dorsal anterior cingulate cortical volume
- increased posterior cingulate cortical volume
- differences in frontal lobe volume

4 Month Behavioral Visit:

Reactivity Assessment: n=41 infants were shown a series of novel visual and auditory stimuli (**Fig. 1**)^{6,11} • video recorded & coded for:

• Beck Anxiety Inventory (BAI)¹² • total maternal anxiety scores at 3-4 mo.

4 Month MRI Visit:

regions of interest (ROI) selected a priori based on regions associated with internalizing problems and higher maternal stress/internalizing disorders in literature (**Fig. 4**)^{4, 7, 8, 9, 10, 14, 15}

- Ο

• Regression analyses were conducted to investigate whether negative affect moderated the relation between maternal anxiety and volume at ROIs, controlling for total intracranial volume.

Maternal Anxiety, Temperament & **Brain Morphometry in Infancy**

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METHODS

- 1. motor activity
- 2. positive affect (i.e., smiling)
- 3. negative affect (i.e., fussing or crying)



Fig. 1. 4-month reactivity assessment

• high-resolution structural MRI data were acquired from infants during natural sleep (T1- and T2-weighted images; **Fig. 2**)

• MRI data were processed using iBEAT structural pipeline to obtain subcortical and cortical volume estimates (**Fig. 3**)¹³

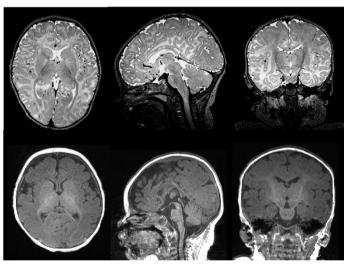


Fig. 2. Raw T2-weighted images (top), raw T-1 weighted images (bottom)

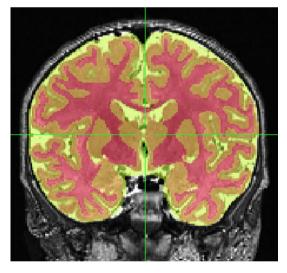


Fig. 3. iBEAT tissue segmentation output

hippocampus

- o 📕 amygdala
- dorsal anterior cingulate cortex
- posterior cingulate cortex
- superior frontal gyrus
- **middle frontal gyrus**
- inferior frontal gyrus

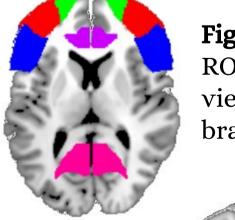
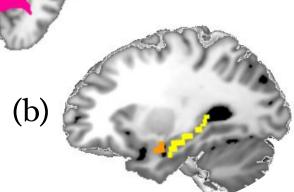


Fig. 4. Highlighted ROIs on axial brain view (a), sagittal brain view (b) ¹⁶







RESULTS

Results indicate that there was no significant interaction and no significant main effect of temperament. However, greater maternal anxiety predicted larger volume in the ROIs below.

Region of Interest	Predictor	β	р	R ²
Hippocampus	Total Brain Volume	.664	.000*	F(4,34)=11.048, p<.000, R ² =.565
	Maternal Anxiety	.417	.036*	
	Negative Affect	1.168	.151	
	Anxiety X Negative	-1.291	.119	
Amygdala	Total Brain Volume	.665	.000*	F(4,34)=11.279, p<.000, R ² =.570
	Maternal Anxiety	.429	.031*	
	Negative Affect	1.127	.163	
	Anxiety X Negative	-1.245	.131	
Dorsal anterior	Total Brain Volume	.659	.000*	F(4,34)=10.609, p<.000, R ² =.555
cingulate cortex	Maternal Anxiety	.416	.039*	
-	Negative Affect	1.140	.165	
	Anxiety X Negative	-1.256	.134	
Posterior cingulate	Total Brain Volume	.661	.000*	F(4,34)=10.786, p<.000, R ² =.559
cortex	Maternal Anxiety	.407	.042*	
	Negative Affect	1.144	.162	
	Anxiety X Negative	-1.270	.128	
Superior frontal	Total Brain Volume	.662	.000*	F(4,34)=10.751, p<.000, R ² =.558
gyrus	Maternal Anxiety	.410	.041*	
	Negative Affect	1.133	.166	
	Anxiety X Negative	-1.252	.133	
Middle frontal	Total Brain Volume	.666	.000*	F(4,34)=11.074, p<.000, R ² =.566
gyrus	Maternal Anxiety	.411	.039*	
	Negative Affect	1.135	.162	
	Anxiety X Negative	-1.256	.129	
Inferior frontal	Total Brain Volume	.678	.000*	F(4,34)=11.664, p<.000, R ² =.578
gyrus	Maternal Anxiety	.404	.039*	
	Negative Affect	1.123	.160	* p<.08
	Anxiety X Negative	-1.241	.128	

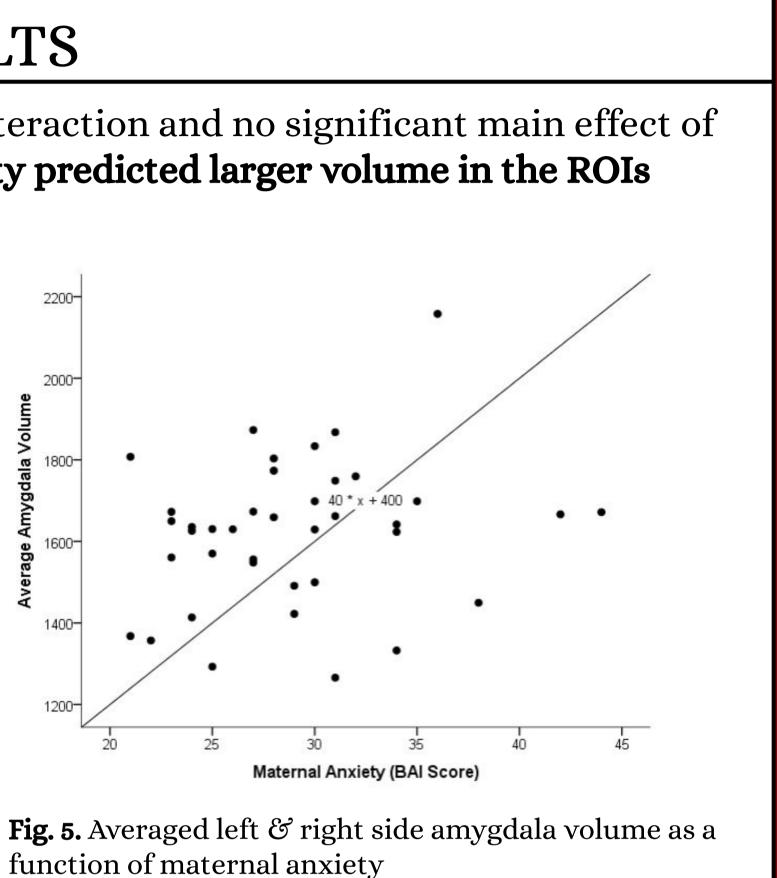


Table 1. Regression results predicting average brain
 volumes at 4 months.

CONCLUSIONS

• Infant brain morphometry was not related to negative affect or the interaction between negative affect and maternal anxiety.

• In line with other studies, maternal anxiety is associated with differences in infant brain morphometry, particularly regions linked to memory, fear, and cognitive control.

FUTURE DIRECTIONS

• Replicate these results using whole-brain analysis and correct for multiple comparisons.

• While this study is a cross-sectional assessment of infant brain structure, it would be interesting to know maternal anxiety predicts changes in these regions over time.

• For example, one recent study shows that postpartum anxiety is correlated with slowed growth of the hippocampus.¹⁰

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REFERENCES

) Feldman, R., Granat, A., Pariente, C., Kanety, H., Kuint, J., & Gilboa-Schechtman, E. (2009). Journal of the American Academy of Child & Adolesce Psychiatry, 48(9), 919-927 (3) Britton, J. R. (2011). Women & Health, 51(1), 55-71.) Buss, C., Davis, E. P., Shahbaba, B., Pruessner, J. C., Head, K., & Sandman, C. A. (2012). Proceedings of the National Academy of Sciences, 201 (5) Clauss, J. A., & Blackford, J. U. (2012). Journal of the American Academy of Child & Adolescent Psychiatry, 51(10), 1066-1075 (6) Fox, N. A., Snidman, N., Haas, S. A., Degnan, K. A., & Kagan, I. (2015). Infancy, 20(1), 98-114. (7) Ducharme, S., Albaugh, M. D., Hudziak, J. J., Botteron, K. N., Nguyen, T. V., Truong, C., ...& Schapiro, M. (2013). Cerebral cortex, 24(11), 2941-2950. (8) Schwartz, C. E., Kunwar, P. S., Greve, D. N., Moran, L. R., Viner, J. C., Covino, J. M., ... & Wallace, S. R. (2010). Archives of general psychiatry, 67(1), 78-84. (9) Sylvester, C. M., Barch, D. M., Harms, M. P., Belden, A. C., Oakberg, T. J., Gold, A. L., ...& Henderson, H. A. (2016). Journal of the American Academy of Child & Adolescent Psychiatry, 55(2), 122-129 (10) Schwartz, C. E., Kunwar, P. S., Hirshfeld-Becker, D. R., Henin, A., Vangel, M. G., Rauch, S. L., ... & Rosenbaum, J. F. (2015). Translational psychiatry, 5(7), e605. 11) Kagan, J., & Snidman, N. (1991). Temperamental factors in human development. American Psychologist, 46(8), 856. (12) Beck, A. T., Epstein, N., Brown, G., & Steer, R. A. (1988). Journal of consulting and clinical psychology, 56(6), 893. (13) Dai, Y., Shi, F., Wang, L., Wu, G., & Shen, D. (2013). Neuroinformatics, 11(2), 211-225. (14) Qiu, A., Rifkin-Graboi, A., Chen, H., Chong, Y. S., Kwek, K., Gluckman, P. D., ... & Meaney, M. J. (2013). Translational psychiatry, 3(9), e306. (15) Gold, A. L., Steuber, E. R., White, L. K., Pacheco, J., Sachs, J. F., Pagliaccio, D., ... & Pine, D. S. (2017). Neuropsychopharmacology, 42(12), 2423-2433. 16) Lancaster, J. L., Cykowski, M. D., McKay, D. R., Kochunov, P. V., Fox, P. T., Rogers, W., ... & Mazziotta, J. (2010). Neuroinformatics, 8(3), 171-182.