Correction for Orellana et al., childhood maltreatment influences adult brain structure through its effects on immune, metabolic, and psychosocial factors

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Note: To cite this publication please use the final published version (if applicable).

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Correction for "Childhood maltreatment influences adult brain structure through its effects on immune, metabolic, and psychosocial factors," by Sofia C. Orellana, Richard A. I. Bethlehem, Ivan L. Simpson-Kent, Anne-Laura van Harmelen, Petra E. Vértes, and Edward T. Bullmore which published April 9, 2024; 10.1073/pnas.2304704121 (*Proc. Natl. Acad. Sci. U.S.A.* **121**, e2304704121).

The authors note: "During corrections of the paper in response to reviewer comments, Fig. 2 was accidentally swapped with an earlier version of the same figure where the data used to compute the linear models of the relationships between BMI, CRP, AT, and cortical thickness and subcortical volume had not been log transformed. In the correct and newer version of Fig. 2, showing the results of analysis of appropriately log-transformed data, results remain largely unchanged. There are only small changes in magnitude for the segments of the plot associated with AT: 1) in the brain plot for "Brain ~ AT" (Fig. 2 *A, Bottom Left*) where the magnitude of the color bar limits decreases by approximately 1 unit; 2) In the scatterplot of AT values vs. CT/volume in the regions with biggest linear effects (Fig. 2 *A, Middle Bottom*), the correlation magnitudes change; and 3) in the scatterplots of effect sizes (t-values) of AT (y-axis) vs. BMI effect sizes (t-values, x-axis) the depicted correlation
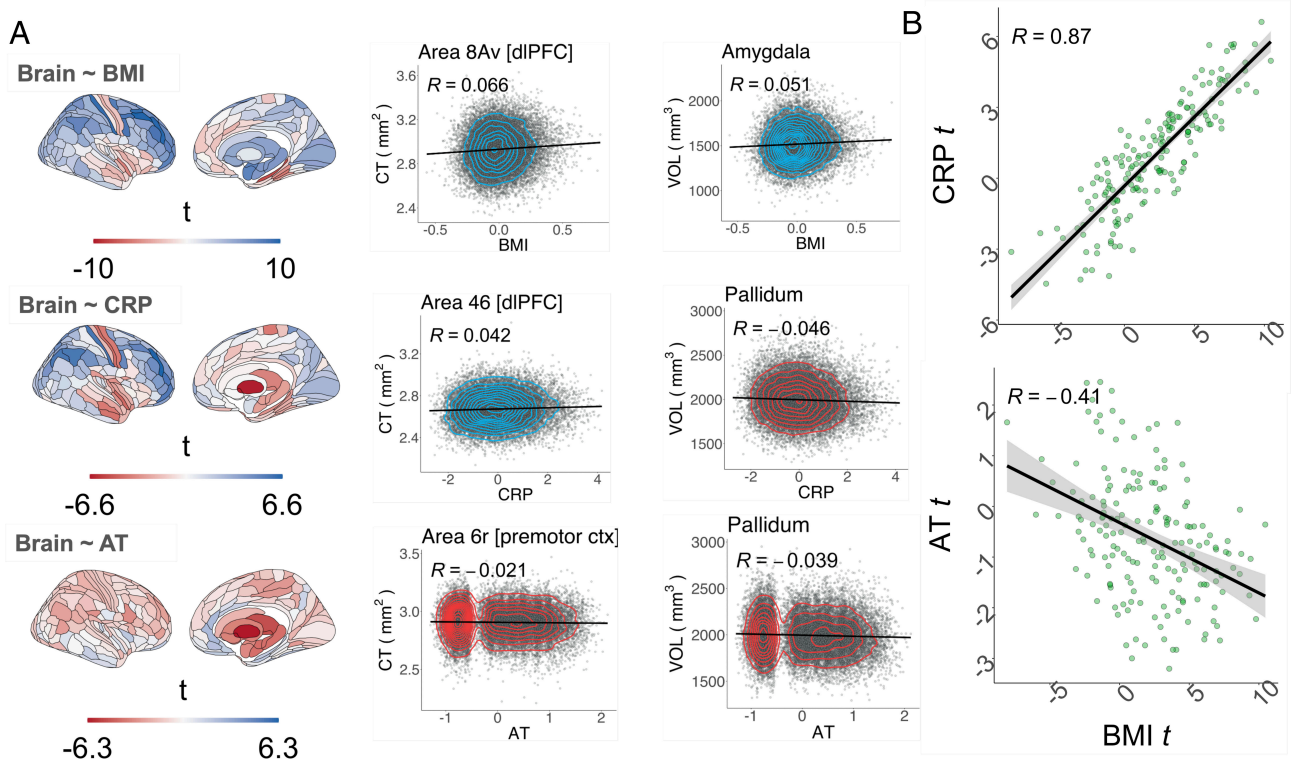

Fig. 2. Independent effects of adult trauma, BMI, and CRP on adult cortical thickness and subcortical volumes. (*A, Left column*) Brain maps of independent linear relationships between adult trauma (AT), CRP or BMI, and cortical thickness (CT) and subcortical volume. Each map shows the anatomical distribution of effect sizes (*t*-values); for corresponding maps thresholded for FDR-corrected significance, see *SI Appendix*, Fig. S18; for maps of standardized regression β coefficients, see SF20A&B. Negative *t*-values indicate a reduction in either cortical thickness or subcortical volume (red), and positive *t*-values indicate an increase in gray matter (blue), as a result of increase in one of these independently treated predictor variables. (*A, Right column*) Illustrative scatterplots of the relationship between each independent variable and the cortical area or subcortical structure most strongly associated with it. Cortical areas are labeled by their specific areal nomenclature and corresponding regional grouping, as defined by the Glasser template (35). (*B, Top*) Scatterplot of the effect size (*t*-value) of BMI (*x*-axis) versus the effect size of CRP (*t*-value; *y*-axis) on cortical thickness; each point represents one of 180 cortical areas; Spearman's correlation $\rho = 0.87$, $P_{spin} < 0.0001$ over all areas; the solid line is the regression of *t*-values for the effect of BMI on *t*-values for the effect of CRP. (*B, Bottom*) Scatterplot of the effect size of BMI on CT (*x*-axis) versus the effect size of AT on CT (*y*-axis); Spearman's $\rho = -0.41$, $P_{spin} = 0.0009$.
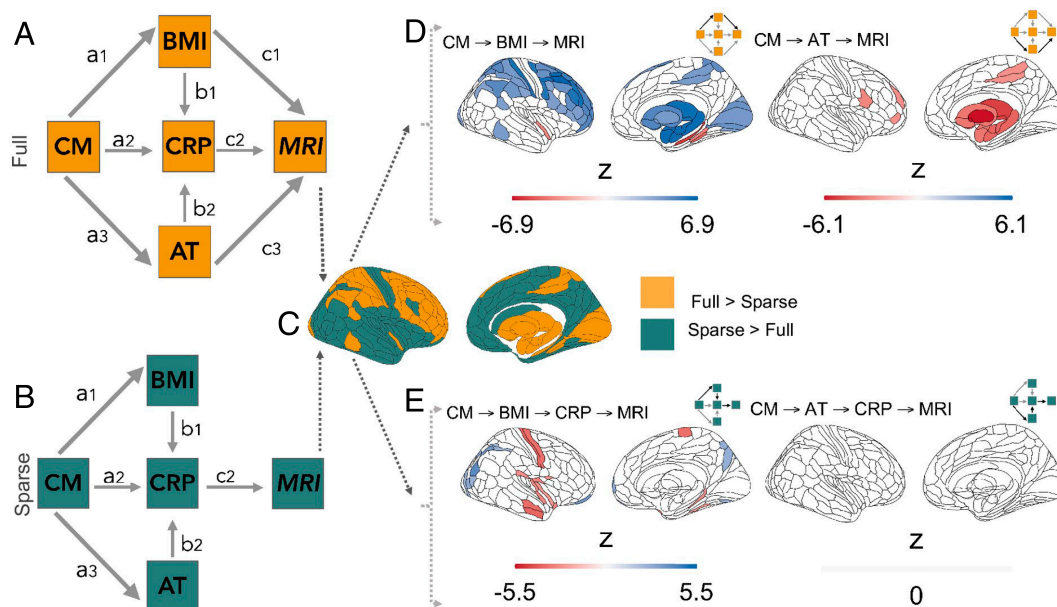
Fig. 3. Indirect effects of childhood maltreatment (CM) on cortical subcortical structures can be mediated by direct effects on body mass index (BMI), C-reactive protein (CRP), or adult trauma (AT) in two nested path models (full and sparse). (*A* and *B*) Diagrams of nested path models of indirect effects of CM on brain structure. Full model (*A*): contains direct effects of BMI, CRP, and AT on adult brain MRI measurements (paths c1, c2, and c3, respectively); all other paths between non-MRI variables are identical to the model in Fig. 1. Sparse model (*B*) contains a direct effect of CRP, only, on adult brain structure; adult trauma and BMI can have indirect effects on brain MRI measurements mediated by their direct effects on CRP. (*C*) Comparison of full and sparse models: This pair of nested models was evaluated at each of 180 cortical areas defined by the Glasser parcellation (36) and their difference in model goodness-of-fit was measured by the likelihood-ratio. Yellow areas indicate significantly better fit by the full model at FDR ≤ 0.05; green areas indicate where the sparse model was sufficient to explain local variance. (*D, Left*) Brain map of BMI-mediated indirect effects (Wald z) of childhood maltreatment on brain structure, together with a schema highlighting (in bold lines) the paths whose coefficients are combined to estimate the overall magnitude of the indirect effect. Blank areas on the cortical and subcortical maps indicate nonsignificant results (FDR ≥ 0.05) or locations where the model was not evaluated. Negative z-values indicate decreased gray matter (red), and positive z-values indicate increased gray matter (blue), associated with greater BMI predicted by greater CM. (*D, Right*) Indirect effects of childhood maltreatment on brain structure, mediated by adult trauma. Negative z-values indicate decreased gray matter (red); positive z-values indicate increased gray matter (blue), associated with greater AT predicted by greater CM. For thresholded and unthresholded maps of all paths evaluated see *SI Appendix*, Figs. S21 and S22; and for unstandardized coefficients see *SI Appendix*, Figs. S23 and S24. (*E, Left*) Childhood maltreatment had indirect effects on adult brain structure that were mediated by a chain of paths from CM → BMI → CRP. Negative z-values indicate reduced CT was indirectly predicted by CM via its direct effects on BMI, which in turn could have effects on brain structure directly or via its effects on CRP. (*E, Right*) There were no significant indirect effects of childhood maltreatment mediated by a chain of paths from CM to CRP via AT, i.e., CM → AT → CRP. For maps of all thresholded and unthresholded paths see *SI Appendix*, Figs. S25 and S26; for unstandardized coefficients *SI Appendix*, Figs. S27 and S28. Wald z scores represent the product of path coefficients (standardized by their standard errors) constituting each of the indirect effects of CM on brain structure evaluated by these two (full and sparse) models.

also changes slightly. Additionally, while Fig. 3 is correct in its entirety, there is a minor typing error in the writing of the caption where the mapping of the colors on the brain maps, to their corresponding sign, is swapped. Here, red should indicate decreases while blue should indicate increases. The correct color mapping is displayed in the color bars under the brain maps of the figure itself."

These errors were discovered while re-formatting the contents of the paper to be included in the first author's PhD thesis. Regarding Fig. 2, the authors explain, "There is no change in any of the results from statistical significance to nonsignificance, and there is no impact on any of the substantive conclusions of the paper, which remain correct as currently stated. The only impact on the informed reader is that they might notice that the current version of Fig. 2 shows data plotted on a natural scale, but the text of the paper correctly describes analysis of log-transformed data." Regarding Fig. 3, the authors explain, "The rest of the paper, and the figure itself, are correct and consistent in their use of the color red to indicate decreases in brain structure and blue to indicate increases. No results in the paper are affected by this typing error."

As noted above by the authors Fig. 2 appeared incorrectly. The corrected figure and its legend appear below.

As noted above by the authors as well, the legend for Fig. 3 appeared incorrectly. The figure and its corrected legend appear below. The portion of the Fig. 3 legend "…Negative z-values indicate decreased grey matter (blue), and positive z-values indicate increased grey matter (red), associated with greater BMI predicted by greater CM. (*D, Right*) Indirect effects of childhood maltreatment on brain structure, mediated by adult trauma. Negative z-values indicate decreased grey matter (blue); positive z-values indicate increased grey matter (red), associated with greater AT predicted by greater CM. For thresholded and unthresholded maps of all paths evaluated see *SI Appendix*, Figs. S21 and S22; and for unstandardized coefficients see *SI Appendix*, Figs. S23 and S24…" should instead appear as, "Negative z-values indicate decreased gray matter (red), and positive z-values indicate increased gray matter (blue), associated with greater BMI predicted by greater CM. (*D, Right*) Indirect effects of childhood maltreatment on brain structure, mediated by adult trauma. Negative z-values indicate decreased gray matter (red); positive z-values indicate increased gray matter (blue), associated with greater AT predicted by greater CM. For thresholded and unthresholded maps of all paths evaluated see *SI Appendix*, Figs. S21 and S22; and for unstandardized coefficients see *SI Appendix*, Figs. S23 and S24…"

The online version of Figs. 2 and the legend to Fig. 3 have been corrected.