**Supplementary material**

Fares-Otero, N.E. et al. (2024). Triangulating the associations of different types of childhood adversity and first-episode psychosis with cortical thickness across brain regions

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# **S1. Further clinical assessment and reliability of the instruments**

Clinical symptom severity was assessed using the adapted Spanish version (Kay, Fiszbein, Vital-Herne, & Fuentes, 1990) of the Positive and Negative Syndrome Scale (PANSS) (Kay, Fiszbein, & Opler, 1987) on a 7-point Likert-scale which represents increasing levels of psychopathology (from 1 = absent to 7 = extreme). The total score as well as the positive, negative, and general psychopathology dimensions were calculated. For each scale, the items were summed to obtain a total score, with higher scores indicating greater severity. The PANSS is a widely used measure with high internal consistency and test–retest reliability, and it has shown a very satisfactory internal consistency in our sample. The Cronbach’s alpha coefficients for each dimension were: α = 0.87 for the positive scale, α = 0.91 for the negative scale, and α = 0.91 for the general scale.

The intensity of manic symptoms was assessed using the Young Mania Rating Scale (YMRS) (Young, Biggs, Ziegler, & Meyer, 1978), which comprises 11 items rated on a 5-point Likert-scale. The total score was calculated and the internal consistency in our sample was α = 0.82.

Depression severity was assessed using the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960). The HDRS scale contains 21 items distributed in a 3- or 5-point Likert-scale and a global score. In the present study, the internal consistency was α = 0.89 for the global scale.

In addition, the severity of the patient's illness at the time of assessment was assessed with the Clinical Global Impression Scale (CGI-S) (Guy, 1976), a 7-point scale that the clinician must rate. Finally, the duration of untreated psychosis (DUP) was calculated as the number of days between the first manifestation of psychotic symptoms and the initiation of psychiatric (or adequate pharmacological) treatment (Norman & Malla, 2001).

Global functioning was assessed using the Global Assessment of Functioning (GAF), which combines the clinical judgment of symptoms as well as relational, social, and occupational functioning on a single axis ranging from 1 (severely impaired) to 100 (extremely high functioning). The GAF score is a reliable measure of global functioning in adults with psychotic disorders (Startup, Jackson, & Bendix, 2002). Alternatively, the Child Global Assessment Scale (C-GAS) was used to provide a global measure of the level of functioning in children and adolescents (Shaffer et al., 1983).

# **Table S2. *Frequencies of CAs in affective and non-affective FEP***

|  |  |  |
| --- | --- | --- |
| **Childhood adversities** | **non-affective FEP n = 93** | **affective FEP****n = 23** |
| Any adversity | 64(69.6%) | 19(82.6%) |
| Overall maltreatment  | 24(26.7%) | 7(30.4%) |
| Emotional abuse | 14(15.2%) | 4(17.4%) |
| Physical abuse | 15(16.5%) | 5(21.7%) |
| Sexual abuse | 7(7.8%) | 0(0%) |
| Neglect (emotional and physical) | 6(6.6%) | 2(8.7%) |
| Threat | 51 (54.8%) | 15(65.2%) |
| Deprivation | 44 (47.8%) | 12 (52.2%) |
| Parental discord  | 39(42.9%) | 10(43.5%) |
| Parental death | 4(4.3%) | 1(4.3%) |
| Separation from parents  | 31(33.7%) | 10(43.5%) |
| Expelled from school | 15(16.5%) | 7(30.4%) |
| Household poverty | 25(28.1%) | 6(26.1%) |
| Overall bullying  | 23(24.7%) | 7(30.4%) |
|  Emotional bullying | 22(23.7%) | 5(21.7%) |
|  Physical bullying | 8(8.6%) | 5(21.7%) |

***Note.*** CAs: Childhood adversities; FEP: First-episode psychosis;Affective FEP includes type 1 bipolar disorder or major depressive disorder with psychotic symptoms; non-affective FEP includes schizophrenia spectrum disorders (schizophrenia, schizophreniform) and other psychoses; Emotional bullying includes verbal/relational victimisation.

# **Table S3**. ***Correlations between the brain map of CA effects and the brain map of FEP effects***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Childhood adversities** | ***n* HC** | ***n* CAs** | ***n* FEP**  | ***r*** | ***p*** |
|  |  |  |  |  |  |
| **Any adversity**  | **13** | **83** | **32** | **0.82** | **<0.001** |
| **Separation from parents**  | **71** | **26** | **74** | **0.50** | **<0.001** |
| **Emotional bullying**  | **73** | **25** | **89** | **0.48** | **<0.001** |
| **Threat**  | **32** | **66** | **49** | **0.54** | **<0.001** |
| **Overall bullying**  | **71** | **27** | **88** | **0.40** | **<0.001** |
| **Parental discord** | **52** | **46** | **65** | **0.37** | **0.002** |
| **Deprivation**  | **50** | **46** | **56** | **0.32** | **0.008** |
| **Household poverty**  | **64** | **33** | **81** | **0.27** | **0.024** |
| **Sexual abuse**  | **87** | **11** | **106** | **0.25** | **0.039** |
| Expelled from school | 76 | 22 | 92 | 0.23 | 0.061 |
| Overall maltreatment  | 57 | 40 | 82 | 0.19 | 0.121 |
| Emotional abuse | 71 | 27 | 97 | 0.19 | 0.125 |
| Physical bullying  | 91 | 7 | 103 | 0.13 | 0.279 |
| Physical abuse | 79 | 18 | 94 | 0.12 | 0.323 |
| Parental death | 95 | 3 | 111 | 0.06 | 0.627 |
| Neglect  | 89 | 9 | 106 | -0.02 | 0.874 |

***Note****.* CA: Childhood adversities; Correlations between brain map of CA effects (in HCs) and brain map of FEP effects (in non-CAs); FEP: First-episode psychosis; HC: Healthy controls; *n* = cortical thicknesseffects; p-values adjusted by age and sex, significant at *p* < 0.05; Threat includes experiences involving harm or threat of harm (i.e. physical and/or sexual abuse). Deprivation is the absence of expected inputs from the environment or absence of stimulation that occurs in the context of caregiver interactions (i.e., household poverty, neglect, separation from parents); Emotional bullying includes verbal/relational victimisation.

# **Table S4. *Correlations between the brain map of CA effects and the brain map of FEP effects in non-affective and affective psychosis***

|  |  |
| --- | --- |
| Non-affective first-episode psychosis | Affective first-episode psychosis |
|  CAs n HCs n CAs n FEP r *p* **Any adversity 13 83 28 0.806 <0.001** **Threat 32 66 41 0.486 <0.001****Separation from parents 71 26 61 0.460 <0.001** **Emotional bullying 73 25 71 0.457 <0.001** **Parental discord 52 46 52 0.318 0.008** **Overall bullying 64 34 70 0.316 0.009** **Deprivation 50 46 45 0.272 0.025** **Household poverty 64 33 64 0.249 0.040****Expelled from school 76 22 76 0.240 0.049** Abuse 60 37 68 0.204 0.095 Sexual abuse 87 11 83 0.201 0.100Overall maltreatment 57 40 66 0.180 0.141 Emotional abuse 71 27 78 0.173 0.158 Parental death 95 3 89 0.090 0.467 Physical abuse 79 18 76 0.088 0.478 Physical bullying 91 7 85 0.053 0.668 Neglect 89 9 85 -0.024 0.846 |  CAs n HCs n CAs n FEP r *p* **Any adversity 13 83 4 0.644 <0.001** **Threat 32 66 8 0.554 <0.001** **Emotional bullying 73 25 18 0.474 <0.001 Separation from parents 71 26 13 0.405 <0.001** **Parental discord 52 46 13 0.403 <0.001** **Overall bullying 64 34 16 0.330 0.006** **Physical bullying 91 7 18 0.308 0.011** **Deprivation 50 46 11 0.295 0.015** **Sexual abuse 87 11 23 0.288 0.017** **Household poverty 64 33 17 0.250 0.040** Abuse 60 37 17 0.201 0.101 Emotional abuse 71 27 19 0.164 0.180 Physical abuse 79 18 18 0.127 0.302Overall maltreatment 57 40 16 0.120 0.329Expelled from school 76 22 16 0.100 0.418 Parental death 95 3 22 -0.032 0.793 Neglect 89 9 21 -0.011 0.927 |

***Note.*** CAs: Childhood adversities; HCs: Healthy controls (without first-episode psychosis); FEP: first-episode psychosis; Threat involves experiences of harm or threat of harm (i.e., physical and sexual abuse, parental discord), Abuse involves all types of abuse (i.e., physical, emotional, sexual); Deprivation is the absence of expected inputs from the environment or absence of stimulation that occurs in the context of caregiver interactions (i.e., household poverty, neglect, separation from parents); Neglect involves emotional and/or physical neglect; Emotional bullying includes verbal/relational victimisation.

# **S5. Interaction effects of FEP and CA on cortical thickness**

## **Table S5.1. *Associations between different types of CAs and FEP***

|  |  |
| --- | --- |
| Non-affective FEP | Affective FEP\* |
| Childhood adversities p any\_adversity 0.008  threat 0.042overall\_maltreatment 0.045 | - |

 ***Note.*** CA: childhood adversity; FEP: First-episode psychosis;HC: Healthy

 controls; \*No association between any CA and affective FEP was observed.

## **Table S5.2 *Associations between FEP and cortical thickness***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cortical region** | ***b*** | **95% CIs** | ***t*** | ***p*** | ***p corr*** |
| rh lateral occipital | -0.08 | [-0.10, -0.05] | -5.2 | **<0.001** | **<0.001** |
| rh caudal middle frontal | -0.09 | [-0.12, -0.05] | -4.6 | **<0.001** | **0.001** |
| rh superior frontal | -0.08 | [-0.12, -0.05] | -4.5 | **<0.001** | **0.001** |
| lh caudal middle frontal | -0.08 | [-0.10, -0.05] | -5.2 | **<0.001** | **<0.001** |
| rh parsorbitalis | -0.10 | [-0.15, -0.06] | -4.3 | **<0.001** | **0.002** |
| rh middle temporal | -0.08 | [-0.11, -0.04] | -4.3 | **<0.001** | **0.002** |
| lh superior frontal | -0.07 | [-0.10, -0.04] | -4.2 | **<0.001** | **0.003** |
| lh middle temporal | -0.07 | [-0.11, -0.04] | -4.1 | **<0.001** | **0.004** |
| lh postcentral | -0.06 | [-0.09, -0.03] | -4.0 | **<0.001** | **0.006** |
| rh parsopercularis | -0.08 | [-0.12, -0.04] | -4.0 | **<0.001** | **0.006** |
| lh lateral occipital | -0.05 | [-0.08, -0.03] | -3.7 | **<0.001** | **0.017** |
| lh lateral orbitofrontal | -0.07 | [-0.10, -0.03] | -3.6 | **<0.001** | **0.022** |
| rh precuneus | -0.06 | [-0.09, -0.03] | -3.6 | **<0.001** | **0.025** |
| lh supramarginal | -0.06 | [-0.10, -0.03] | -3.5 | **0.001** | **0.033** |
| rh inferior parietal | -0.05 | [-0.08, -0.02] | -3.4 | **0.001** | **0.039** |
| lh transverse temporal | -0.09 | [-0.15, -0.04] | -3.4 | **0.001** | **0.039** |
| lh inferior parietal | -0.05 | [-0.08, -0.02] | -3.4 | **0.001** | **0.039** |

***Note.*** FEP: First-episode psychosis;rh: right hemisphere; lh: left hemisphere; CIs: confidence intervals; significant at *p* < 0.05; *p corr*: corrected *p-*values adjusted by age and sex.

## **Table S5.3 *Associations between FEP and cortical thickness in non-affective and affective psychosis***

|  |  |
| --- | --- |
| Non-affective FEP | Affective FEP\* |
|  mri b b\_lo b\_up t *p pcorr* rh\_lateraloccipital\_thickness -0.07 -0.10 -0.05 -4.9 <0.001 <0.001 lh\_middletemporal\_thickness -0.08 -0.12 -0.05 -4.6 <0.001 0.001 rh\_parsorbitalis\_thickness -0.11 -0.16 -0.06 -4.5 <0.001 0.001 rh\_superiorfrontal\_thickness -0.09 -0.13 -0.05 -4.5 <0.001 0.001 rh\_caudalmiddlefrontal\_thickness -0.09 -0.13 -0.05 -4.4 <0.001 0.001 rh\_middletemporal\_thickness -0.08 -0.12 -0.04 -4.4 <0.001 0.001 lh\_caudalmiddlefrontal\_thickness -0.09 -0.13 -0.05 -4.3 <0.001 0.001 lh\_superiorfrontal\_thickness -0.08 -0.11 -0.04 -4.3 <0.001 0.002 rh\_parsopercularis\_thickness -0.09 -0.14 -0.05 -4.2 <0.001 0.002 lh\_postcentral\_thickness -0.06 -0.09 -0.03 -4.1 <0.001 0.004lh\_lateralorbitofrontal\_thickness -0.07 -0.11 -0.03 -3.9 <0.001 0.009 rh\_inferiorparietal\_thickness -0.06 -0.09 -0.03 -3.8 <0.001 0.010 lh\_bankssts\_thickness -0.09 -0.13 -0.04 -3.7 <0.001 0.015 lh\_transversetemporal\_thickness -0.11 -0.17 -0.05 -3.7 <0.001 0.016 lh\_parstriangularis\_thickness -0.07 -0.11 -0.04 -3.7 <0.001 0.016 rh\_parstriangularis\_thickness -0.08 -0.12 -0.04 -3.6 <0.001 0.023 rh\_precuneus\_thickness -0.06 -0.09 -0.03 -3.6 <0.001 0.024 lh\_supramarginal\_thickness -0.06 -0.10 -0.03 -3.6 <0.001 0.025 lh\_precentral\_thickness -0.06 -0.09 -0.02 -3.5 0.001 0.033 lh\_inferiorparietal\_thickness -0.05 -0.09 -0.02 -3.4 0.001 0.036 rh\_superiortemporal\_thickness -0.07 -0.11 -0.03 -3.4 0.001 0.039 | - |

 ***Note.*** FEP: First-episode psychosis;mri: magnetic resonance imaging, rh:

 right hemisphere, lh: left hemisphere, b lo: lower bound; b up: upper bound;

 pcorr: corrected *p*-values by sex and age. \*No association between affective

 FEP and cortical thickness was observed.



# ***Fig. S1*. Interaction effects of bullying and FEP on cortical thickness in individuals with affective psychosis**

***Note.*** FEP: first-episode psychosis); light blue represents cortical thinning; orange represents cortical thickening. A significant interaction effect was observed between experiencing affective FEP and exposure to emotional bullying (verbal/relational victimisation), which was associated with thickening in the right posterior cingulate cortex (*β =* 0.34, [0.19, 0.49], *p*corr = .002).

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