Supplemental Material

Methods

Childhood Trauma Assessment

The modified version of Childhood Experience of Care and Abuse (CECA) Questionnaire included information about loss of parents, separation from parents for more than 6 months, and physical and sexual abuse occurred before the age of 17 years. A composite variable was created using the four dichotomized variables (loss of parents, separation from parents for more than 6 months, severe physical abuse and presence of sexual abuse): the score of this variable ranged between 0 (absence of any childhood trauma) to 4 (presence of all four childhood traumas investigated).

Magnetic Resonance Imaging

The whole brain was scanned with an axial inversion recovery prepared SPGR volume. TR was 11.2 ms, TI was 300 ms, TE was 4.8 ms, and the flip angle was 18 degrees, slice thickness was 1.1 mm. The images were obtained with in plane resolution 1.1mmx1.1mm, in 280x280 mm field of view.

Gene expression analyses

The RNA quantity was assessed by evaluation of the A260/280 and A260/230 ratios using a Nanodrop spectrometer (NanoDrop Technologies, Wilmington, DE, USA), and the RNA quality was determined using an Agilent Bioanalyzer (Agilent Technologies Italia S.p.A. Cernusco sul Naviglio, MI, Italy). Two micrograms of total RNA were then used for cDNA synthesis and for subsequent gene expression analysis in Real Time PCR. Quantitative Real-Time PCR was performed using HOT FIREPol® EvaGreen® qPCR Mix (Solis BioDyne, Tartu, Estonia) according to the

SYBR Green method. For each target primer set, a validation experiment was performed to demonstrate that PCR efficiencies were within the range of 90-100% and approximately equal to the efficiencies of the reference genes (glyceraldehyde 3-phosphate dehydrogenase (GAPDH), beta-actin (ACTB) and beta-2-microglobulin (B2M)). Briefly, after an initial heating step at 95°C for 15 min to activate the polymerase, 45 PCR cycles were performed. Each cycle consisted of a denaturation step at 95°C for 30 s, an annealing step at 60°C for 30 s and an elongation step at 72°C for 30 s. Each sample was assayed in duplicate and each target gene (BDNF, IL-6 and TNF-alpha) was normalized to the gene expression of the three reference genes: GAPDH, ACTB and B2M. The primers used to analyze BDNF gene expression levels have been designed in the BDNF coding region, therefore able to detect all the BDNF splice variants (primer Fw: TGGCTGACACTTTCGAACAC: primer Rw: AGAAGAGGAGGCTCCAAAGG). Pfaffl Method was used to determine relative target gene expression. Data were normalized to the geometric mean of all three reference genes and expressed as Relative Expression Ratio (R).

Results

Table S1: Exploratory correlation analyses with BDNF gene expression in first-episode psychosis patients and in healthy controls.

	BDNF expression in patients	BDNF expression in controls
N. childhood trauma	**rho=-0.42, p=0.006**	rho=-0.1, p=0.6
N. recent stressors	**rho=-0.32, p=0.03**	rho=-0.35, p=0.06
Perceived stress scale	r=-0.23, p=0.1	r=0.01, p=1.0
IL-6 expression	**r=-0.33, p=0.02**	r=0.19, p=0.4
TNF-alpha expression	r=-0.09, p=0.6	r=0.27, p=0.2
Diurnal cortisol levels	r=0.07, p=0.7	r=-0.03, p=0.9
Days of antipsychotic treatment	r=0.06, p=0.7	---

Table S2: Exploratory correlation analyses with left hippocampal volume in first-episode psychosis.

	Left Hippocampal volume
N. childhood trauma	rho=0.27, p=0.3
N. recent stressors	rho=0.10, p=0.7
Perceived stress scale	r=0.09, p=0.7
IL-6 expression	**r=-0.45, p=0.04**
TNF-alpha expression	r=-0.31, p=0.2
BDNF expression	**r=0.53, p=0.01**
Diurnal cortisol levels	**r=-0.68, p=0.001**