Childhood Trauma and Hippocampal and Amygdalar Volumes in First-Episode Psychosis


Published in:
Schizophrenia Bulletin

Document Version:
Peer reviewed version

Queen's University Belfast - Research Portal:
Link to publication record in Queen's University Belfast Research Portal

General rights
Copyright for the publications made accessible via the Queen's University Belfast Research Portal is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The Research Portal is Queen's institutional repository that provides access to Queen's research output. Every effort has been made to ensure that content in the Research Portal does not infringe any person’s rights, or applicable UK laws. If you discover content in the Research Portal that you believe breaches copyright or violates any law, please contact openaccess@qub.ac.uk.
Childhood Trauma and Hippocampal and Amygdalar Volumes in First-Episode Psychosis

Katrina Hoy1, Suzanne Barrett2, Ciaran Shannon*,1, Clodagh Campbell1, David Watson3, Teresa Rushe4, Mark Shevlin4, Feng Bai5, Stephen Cooper2, and Ciaran Mulholland2

1School of Psychology, Queen’s University Belfast, Belfast, N. Ireland; 2Department of Psychiatry, Queen’s University Belfast, Belfast, N. Ireland; 3Computational Neuroscience, University of Ulster, Londonderry, N. Ireland; 4Psychology, University of Ulster, Londonderry, N. Ireland; 5School of Medicine, South East University, Nanjing, China

*To whom correspondence should be addressed; tel: +44-28- 90975447, fax: +44-28-90974222, e-mail: ciaran.shannon@qub.ac.uk

Objective: A history of childhood trauma is common in individuals who later develop psychosis. Similar neuroanatomical abnormalities are observed in people who have been exposed to childhood trauma and people with psychosis. However, the relationship between childhood trauma and such abnormalities in psychosis has not been investigated. This study aimed to explore the association between the experience of childhood trauma and hippocampal and amygdalar volumes in a first-episode psychosis (FEP) population.

Methods: The study employed an observational retrospective design. Twenty-one individuals, who had previously undergone magnetic resonance imaging procedures as part of the longitudinal Northern Ireland First-Episode Psychosis Study, completed measures assessing traumatic experiences and were included in the analysis. Data were subject to correlation analyses (r and rpb). Potential confounding variables (age at FEP and delay to scan from recruitment) were selected a priori for inclusion in multiple regression analyses.

Results: There was a high prevalence of lifetime (95%) and childhood (76%) trauma in the sample. The experience of childhood trauma was a significant predictor of left hippocampal volume, although age at FEP also significantly contributed to this model. There was no significant association between predictor variables and right hippocampal volume. The experience of childhood trauma was a significant predictor of right and total amygdalar volumes and the hippocampal/amygdalar complex volume as a whole.

Conclusions: The findings indicate that childhood trauma is associated with neuroanatomical measures in FEP. Future research controlling for childhood traumatic experiences may contribute to explaining brain morphology in people with psychosis.

Key words: psychosis/trauma/hippocampus/amygdala

Introduction

A history of traumatic events, childhood abuse in particular, is common in psychosis populations.1,2 The Traumagenic Neurodevelopmental (TN) model of psychosis3 hypothesizes that abnormal neurodevelopmental processes can originate in traumatic events in childhood. It has been theorized that these traumatic events may lead to biological changes such as a pathological alteration in the hypothalamic-pituitary-adrenal (HPA) axis4 and to the high responsivity to stress observed in a sizeable percentage of people with schizophrenia. The model is based upon research demonstrating a similar profile of neurological and biochemical abnormalities in individuals with schizophrenia and in those exposed to childhood abuse.3 Indeed, a recent test of the TN model indicates greater HPA axis dysregulation, as measured by cortisol levels, in individuals with a diagnosis of schizophrenia abused as children (especially those emotionally abused) as compared with their nonabused counterparts.5

A number of imaging studies have identified similar brain abnormalities in traumatized individuals with a diagnosis of Post-Traumatic Stress Disorder (PTSD).6 Dissociative Identity Disorder,7 Borderline Personality Disorder (BPD),8 and Major Depression9 to those observed in psychosis. This suggests that trauma may have specific effects on the brain. There is also evidence to suggest that early life stressors, such as childhood abuse and neglect, can result in a reduction in the volume of the hippocampus, which is a prominent substrate for glucocorticoid-mediated negative feedback on HPA activity and that this reduction is observable in adulthood.10,11 A large body of research has demonstrated hippocampal volume reductions in schizophrenia,12–14 although some studies are contradictory.15 It is significant, from a neurodevelopmental perspective, that reductions in hippocampal volume have been observed in first-episode schizophrenia12,16 and in
ultrahigh risk (UHR) groups because they cannot be explained as a consequence of medication effects or disease chronicity. Read et al have therefore posited that such structural abnormalities observed in schizophrenia could in fact be caused by childhood trauma. There is also indirect behavioral evidence of greater temporal/hippocampal dysfunction associated with childhood trauma in this population: explicit verbal memory impairments have been reported to be greater in individuals with chronic schizophrenia who have a significant trauma history.18

It has also been suggested that a “critical period” exists for the normative development of an emotional regulatory system that is able to appropriately differentiate threatening from nontreating environmental stimuli and that trauma exposure during development may impact function of the HPA axis through effects at the level of the amygdala.4 While there is evidence of increased limbic functional sensitivity in individuals who have experienced childhood trauma, results regarding amygdalar volumes in traumatized and psychotic groups lack consensus. In people who have experienced childhood abuse, some studies report minor volume reductions, whereas others report significant amygdalar size reductions.19,20 Meta-analyses of magnetic resonance imaging (MRI) findings in schizophrenia provide evidence of amygdalar reductions, but these conflict with more recent research.15

Despite evidence indicating a high prevalence of childhood maltreatment in psychotic populations and neurobiological consequences of such stress, morphometric studies in psychosis have neither reported nor controlled for a history of childhood trauma, opting instead to highlight possible etiological explanations that are vague or reflect biological reductionism. The present study assessed the experience of childhood maltreatment and its association with hippocampal and amygdalar volumes in a subsample of individuals who participated in the longitudinal Northern Ireland First-Episode Psychosis (NIFEPS) study. To our knowledge, this is the only study that has examined the association between childhood trauma and brain morphology in a psychosis sample to date. We hypothesized that the experience of such trauma would significantly predict hippocampal and amygdalar volumes at illness onset in these patients.

Methods

Participants

Participants were recruited from the NIFEPS which recruited cases of first-episode psychosis (FEP) from psychiatric services between January 2004 and December 2004 in the Northern and Belfast Health and Social Care Catchment Areas in Northern Ireland (population: 782 979). From these referrals, 90 participants consented to and underwent MRI scanning procedures. Exclusion criteria were evidence of psychosis resulting from an organic etiology, history of a traumatic brain injury or neurodegenerative disorder, a previous episode of psychosis, evidence of a learning disability, or a contraindication for an MRI (eg, metal in the body around the scan area).

The 90-scanned participants satisfied International Classification of Diseases (10th edition: ICD-10) criteria for schizophrenia/schizoaffective disorder (n = 25), bipolar disorder/mania (n = 24), and psychotic depression (n = 11), while the remainder were “other psychotic disorders” (n = 30).

All available participants with an MRI (from NIFEPS) were invited to take part in the current study through their keyworkers. Ethical approval for this study was obtained from a local research ethics committee regulated by a statutory research governance framework. Written informed consent was obtained from all participants after they had received a complete description of the study. Participants were also excluded if they were unable to participate due to current mental state.

Twenty-seven participants (30%) were lost to follow-up due to not being contactable, relocation, or death. Sixty-three (70%) participants were contacted. Of these, 41 (19 males [46%] and 22 females [54%]) declined to participate. The 21 individuals who participated satisfied ICD-10 criteria for schizophrenia (n = 10), bipolar disorder/mania (n = 3), psychotic depression (n = 2), and “other psychotic diagnoses” (n = 6). One further individual was interviewed but excluded from statistical analysis as they were judged to be an extreme outlier based on their volumetric measurements.

Characteristics for participants are shown in table 1. Those interviewed were relatively similar in respect of age, gender, and gross brain volumes to those who declined to participate (age at first episode [t = 0.67, df = 60, P = .51], gender [X^2 (1) = 0.65, P = .42], white matter [WM] [t = 1.2, df = 60, P = .24], gray matter [GM] [t = 0.9, df = 60, P = .37], and cerebrospinal fluid (CSF) [t = 0.89, df = 60, P = .38]). People who declined interview were less likely to have a diagnosis of schizophrenia but this did not reach significance (Declined Interview—SCZ/Other = 11/30; \( \chi^2 (1) = 2.68, P = .1 \)).

Materials

Symptom Measures. At both the time of MRI scan and administration of trauma measures, depression was measured using the “Beck Depression Inventory (BDI) II” and psychotic symptoms were assessed using the “Positive and Negative Symptom Scale (PANSS).” These measures have good psychometric properties. In addition, we reported on an “excitement-mania” factor from the PANSS (see table 1). At follow-up, the “Dissociative Experiences Scale II” (DES II) was employed to assess for current symptoms of dissociation. This measure has high levels of reliability and validity.

Trauma Measures. “The Traumatic Experiences Checklist” (TEC) was administered to assess traumatic...
experiences. The TEC is a 33-item self-report questionnaire designed to measure 29 types of potential trauma and the perceived impact of these events. The TEC yields a childhood trauma composite score, comprising various domains of trauma (eg, emotional abuse, sexual abuse, physical abuse. “Childhood trauma: is defined as “trauma occurring before the age of 18 y.”). It has been shown to have good levels of reliability and validity.30

“The Post-Traumatic Diagnostic Scale”31 is a 49-item self-report instrument and is designed to aid in the detection and diagnosis of PTSD. It was administered twice to assess for PTSD in relation to the most significant traumatic experiences in childhood and again in adulthood. This measure has been shown to have high levels of test-retest reliability and of validity.32

The experience and impact of civil conflict was assessed using the “Troubles Related Experiences Questionnaire”.33 This is a 30-item self-report questionnaire designed to assess exposure to, and perceived impact of, civil conflict in Northern Ireland in child and adulthood. Preliminary research suggests high internal reliability.33

MRI Procedures and Measurements

MRI Data Acquisition  MRI scans were obtained using a GE Sigma 1.5 T scanner (General Electric, Milwaukee, WI). The scan protocol consisted of a coronal high-resolution T1 volume acquisition, axial dual echo PD/T2, and axial FLAIR scans. All scans were reviewed by a consultant neuroradiologist for gross anomalies. The T1 volume scan was used for regions of interest (ROI) analyses. A 3D Inversion-Recovery-prepared Fast Spoiled Gradient echo (IR-Prepped FSPGR) sequence was used, with the following parameters: TR/TE = 9.6/2.4, TI = 450, FOV = 220 × 165 mm, 0.87 mm pixel size, flip angle 20°, slice thickness 1.5 mm, acquisition time 6 minutes 51 seconds. Two-dimensional DICOM T1 magnetic resonance images were subsequently combined into three-dimensional volume (NifTI file format) and interpolated to create 1 × 1 × 1 mm isotropic voxels using SPM5 (Wellcome Institute, London, UK). All brain images were globally spatially normalized to MNI space to remove gross differences in brain size, position, and orientation. Between-subject head size variance is large so inclusion of a head size measure as a covariate is important in morphometric analysis. It has been shown that spatial normalization is an effective alternative method34 and may have benefits in determining volume differences between populations35 including for the hippocampus.34

Parcellation of the Hippocampus and Amygda

Manual drawing of the 2 structures involved outlining the periphery of the ROI, delineated separately for the left and right hemispheres from the T1-weighted, spatially normalized coronal images lying on a plane perpendicular to the hippocampus major axis. This process was performed in Analyze 7.5 Imaging Software (Biomedical Imaging Resource, Mayo Clinic). All ROIs were drawn by one experienced researcher (F.B.) who was blinded to group membership. A random subset of 5 participants had their structures redrawn (both right and left hippocampi and amygdala) to test consistency of parcellation. The correlation coefficients for

Table 1. Demographic and Clinical Characteristics of Participants

<table>
<thead>
<tr>
<th>n</th>
<th>Gender (female; %)</th>
<th>21</th>
<th>12 (57%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At first episode/time of scan</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at first episode (mean y; SD; range)</td>
<td></td>
<td>31.86</td>
<td>10.35</td>
</tr>
<tr>
<td>Delay to MRI scan from initial presentation to services (mean wk; SD; range)</td>
<td></td>
<td>52.07</td>
<td>39.8</td>
</tr>
<tr>
<td>Medication at scan</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANSS positive symptoms at first presentation (mean; SD)</td>
<td></td>
<td>14.57</td>
<td>4.99</td>
</tr>
<tr>
<td>PANSS negative symptoms at first presentation (mean; SD)</td>
<td></td>
<td>12.43</td>
<td>6.19</td>
</tr>
<tr>
<td>PANSS general symptoms at first presentation (mean; SD)</td>
<td></td>
<td>30</td>
<td>6.68</td>
</tr>
<tr>
<td>PANSS excitement-mania factor at first presentation (mean; SD)</td>
<td></td>
<td>5.14</td>
<td>1.53</td>
</tr>
<tr>
<td>BDI at first presentation (mean; SD)</td>
<td></td>
<td>23</td>
<td>15</td>
</tr>
<tr>
<td>Alcohol (DSM IV dependence/abuse/use/abstention/never used)</td>
<td></td>
<td>2/4/11/2/2</td>
<td></td>
</tr>
</tbody>
</table>

At trauma interview

<table>
<thead>
<tr>
<th>n</th>
<th>Currently employed (yes; %)</th>
<th>8 (38.1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean years; SD; range)</td>
<td></td>
<td>39.52</td>
</tr>
<tr>
<td>PANSS positive symptoms (mean; SD)</td>
<td></td>
<td>11.81</td>
</tr>
<tr>
<td>PANSS negative symptoms (mean; SD)</td>
<td></td>
<td>14.33</td>
</tr>
<tr>
<td>PANSS general symptoms (mean; SD)</td>
<td></td>
<td>32.71</td>
</tr>
<tr>
<td>PANSS excitement-mania factor (mean; SD)</td>
<td></td>
<td>5.25</td>
</tr>
<tr>
<td>Beck depression symptoms (mean; SD)</td>
<td></td>
<td>17.5</td>
</tr>
<tr>
<td>Dissociation symptoms</td>
<td></td>
<td>19.38</td>
</tr>
<tr>
<td>Number of hospital admissions</td>
<td></td>
<td>2.43</td>
</tr>
<tr>
<td>Psychological therapy (any reason; yes)</td>
<td></td>
<td>9 (42.9%)</td>
</tr>
<tr>
<td>Alcohol units (0/1–10 per wk; %)</td>
<td></td>
<td>7/14</td>
</tr>
</tbody>
</table>

Note: PANSS, Positive and Negative Symptoms Scale; BDI, Beck Depression Inventory; MRI, magnetic resonance imaging; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.

*PANSS excitement—mania factor: excitement, hostility, poor impulse control, and uncooperativeness items.28
hippocampus and amygdala volumes were 0.93 and 0.89, respectively. Anatomic guidelines for the hippocampus were based on a standard neuroanatomical atlas. The hippocampal regions measured included the CA1 to CA4 fields of the cornu ammonis, dentate gyrus, the subiculum, the alveus, and the fimbria. Parahippocampal gyrus, tail of the caudate, amygdala, CSF around the hippocampus, and the fornix were excluded. Tracing of the hippocampus started caudally anteriorly in the section where the crura of the fornices depart from the lateral wall of the lateral ventricles and ended rostrally where the hippocampus disappears below the amygdala.

Anatomic guidelines for the delineation of the amygdala were taken after Brierley. The anterior border was identified where the lateral sulcus closed to form the entorhinal sulcus. The posterior border excluded the tail of the caudate nucleus, the globus palladus and putamen, and lateral geniculate body. In cases where the border of the putamen could not be defined clearly, the medial halves of the structures in the roof were included inside the amygdala boundary. The medial border was drawn to include uncus, but the inferior entorhinal cortex to the uncal notch was excluded. The lateral border was defined by the inferior horn of lateral ventricle or adjacent WM. The superior border was drawn: (1) anteriorly, as a straight line laterally from entorhinal sulcus to the fundus of the inferior portion of the circular sulcus of insula; (2) posteriorly, as a straight line laterally from the superolateral aspect of the optic tract to the fundus of the circular sulcus of insula. Finally, the inferior border was defined by the uncal recess of the lateral ventricle.

**Design and Statistical Analyses**

This observational study employed a retrospective correlational design. Examination of the MRI data revealed one participant who was judged to be an outlier by distance (standard residual = 2.54) and by influence (Cook’s distance = 2.51) and was excluded from subsequent analyses. The total childhood trauma composite score from the TEC, assessing severity of childhood trauma, was not normally distributed and hence, simplified to a Yes/No binary variable “Experience of Childhood Trauma” (no childhood trauma group \(n = 5; \) TEC score = 0; childhood trauma group \(n = 16; \) TEC median score = 10 IQR = 3–33.5)) for the purposes of a priori statistical testing using parametric methods. Associations between variables were tested using Pearson’s parametric correlations \((r\) and \(r_{pb}\)). A series of regression analyses were then conducted to determine if 3 predictor variables of theoretical interest (experience of childhood trauma, age at first episode of psychosis, delay to scan) predicted neuroanatomical volumes. “Age at first episode” was added as a covariate as onset of psychosis most commonly occurs in late adolescence/early adulthood, an observation that is often thought to be a reflection of abnormal neurodevelopmental processes. “Delay to scan” was included primarily as a proxy measure for duration of exposure to antipsychotic medication as all participants were commenced on antipsychotics shortly after first presentation to psychiatric services.

**Results**

**Traumatic Experiences**

Twenty participants (95%) reported experiencing one or more traumatic life events (mean = 7, SD = 4.7, range 0–16). Sixteen participants (76%) reported experiencing “childhood trauma” i.e., trauma occurring prior to 18 years, and 5 participants did not (24%). Of those reporting childhood trauma, 5 (31.25%) reported traumatic experiences to have first occurred between age 0–6 years (all reporting further childhood trauma subsequent to this), 10 (62.5%) between 7 and 12 years (7 reporting further childhood trauma between 13 and 18 y), and 1 (6.25%) between 13 and 18 years. There was little evidence in this small sample that a first trauma experienced earlier (0—6 y) rather than later influenced amygdalar or hippocampal volumes in people with a childhood trauma history, hence this variable was not considered further in these analyses. Fisher’s Exact Test indicated that rates of childhood trauma did not significantly differ between participants with a diagnosis of schizophrenia vs ‘other’ diagnoses \((P = 0.31; \) trauma/no trauma: SCZ \(n = 9/1; \) Other 7/4). The sample characteristics in respect of trauma domains (frequencies of events), as assessed by the TEC, are shown in table 2.

In respect of exposure to conflict related to civil conflict, 17 (85%) participants reported experiencing

<table>
<thead>
<tr>
<th>Age Range (y)</th>
<th>Emotional Neglect (%)</th>
<th>Emotional Abuse (%)</th>
<th>Bodily Threat (%)</th>
<th>Sexual Harassment (No Physical Contact) (%)</th>
<th>Sexual Abuse (Physical Contact) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–18</td>
<td>11 (52)</td>
<td>12 (57)</td>
<td>9 (42)</td>
<td>4 (19)</td>
<td>5 (24)</td>
</tr>
<tr>
<td>0–6</td>
<td>4 (19)</td>
<td>3 (14)</td>
<td>1 (5)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>7–12</td>
<td>8 (38)</td>
<td>11 (52)</td>
<td>6 (29)</td>
<td>2 (9)</td>
<td>3 (14)</td>
</tr>
<tr>
<td>13–18</td>
<td>7 (33)</td>
<td>8 (38)</td>
<td>8 (38)</td>
<td>4 (19)</td>
<td>5 (24)</td>
</tr>
</tbody>
</table>

*Note:* TEC, Traumatic Experiences Checklist
left hippocampus was not significant (adjusted $R^2 = .012$; $df$ (3, 17); $F = 0.919$; $P = .453$; predictors—experience of childhood trauma $\beta = -.164$; age at first episode $\beta = -.362$; delay to scan $\beta = -.153$). The regression model for the left hippocampus was however significant, accounting for 45.1% of the variance (adjusted $R^2 = .451$; $df$ (3, 17); $F = 6.468$; $P = .004$). The 2 significant variables within the model were the experience of childhood trauma ($\beta = -.402$, $P = .028$) and age at first episode ($\beta = .446$, $P = .027$). Delay to scan was not significant in this model ($\beta = .2$).

**Amygdala.** The regression model for total amygdala volume was significant, accounting for 27.3% of the variance (adjusted $R^2 = .273$; $df$ (3, 17); $F = 3.5$; $P = .038$). The only significant variable within the model was the experience of childhood trauma ($\beta = -.5$, $P = .019$; age at first episode $\beta = .256$; delay to scan $\beta = .094$). The regression model for right amygdala volume was significant, accounting for 28.4% of the variance (adjusted $R^2 = .284$; $df$ (3, 17); $F = 3.639$; $P = .034$). The significant variable within the model was the experience of childhood trauma ($\beta = -.419$, $P = .042$; age at first episode $\beta = -.358$; delay to scan $\beta = .11$). The regression model for left amygdala volume approached, but did not achieve, significance, and accounted for 18.8% of the variance (adjusted $R^2 = .188$; $df$ (3, 17); $F = 2.545$; $P = .09$). The significant variable within the model was the experience of childhood trauma ($\beta = -.512$, $P = .022$; age at first episode $\beta = .124$; delay to scan $\beta = .066$).

The relationships between childhood trauma composite scores from the TEC (ranked by severity) and neuroanatomical variables were also examined using simple, nonparametric correlations (Spearman’s Rho): all findings were upheld in these secondary analyses.

### Trauma and Symptomatology

Post hoc analyses between childhood trauma experience and symptomatology were conducted to determine whether there was evidence of interrelationships between the experience of childhood trauma, severity of patients’ illness, and volumetric measures. They were primarily conducted to check whether illness severity in the sample could be a potential confounding factor in these analyses. Given the primary purpose of these secondary analyses was conservative (ie, search for confounds), the large number of correlations being conducted and the small sample size, effect sizes of $r > .35$ were considered further.

Results indicated that there were no relationships of note (all $r_{pb} < .35$) between the experience of childhood trauma...
trauma in these participants and their initial, current, or change in, PANSS scores (positive, negative, and general), current dissociation symptoms, current BDI scores, or change in depression once baseline scores were controlled for. BDI scores at presentation correlated with the experience of childhood trauma ($r_{pb} = -.39$) and a number of neuroanatomical volumes: left hippocampus $r = .4$; right amygdala $r = .49$; and total amygdala $r = .44$. These suggested that higher levels of depression at onset was associated with the absence of a childhood trauma history in the patients sampled as well as larger, rather than smaller, anatomical structures, the opposite of what was observed for the experience of childhood trauma. Effects sizes for these relationships were small to moderate however.

Regressions models were then repeated for all anatomical structures with experience of childhood trauma, baseline symptoms, and change in symptoms (ie, baseline positive symptoms, change in positive symptoms, etc.) as predictor variables. These were undertaken to further ensure that the relationship between the experience of childhood trauma and brain volumes could not be accounted for by indicators of greater illness severity in participants. All findings were upheld, aside from when severity of depression at presentation, and change in depression were examined as additional predictor variables in some models. Changes were thought to be best understood with reference to a degree of multicollinearity in, and/or the additional explanatory terms disimproving aspects of, the regression models.

Discussion

To our knowledge, this study represents the first investigation of childhood trauma and brain morphology in psychosis. The use of a FEP group largely eliminates potential study confounders such as disease chronicity and the effects of long-term antipsychotic medication, which may affect brain morphology. Moreover, a recent innovation in MRI modulation techniques that removes the need to control for brain size was utilized.

The findings support our hypothesized association between the experience of childhood trauma and decreased hippocampal volume, particularly left hippocampal volume. Decreased right, left, and total amygdala volumes were also associated with the experience of childhood traumatic experiences against a background of minimal evidence of amygdalar volume alteration in these patients relative to healthy controls. It would be hypothesized from these data that amygdalar volume enlargement would most likely be observed in psychosis samples with a negligible history of childhood trauma, while no change, or volumetric reductions in the amygdala, would be observable in those cohorts with a high prevalence of childhood trauma. Hence, the findings represent evidence that the neuroanatomical abnormalities observed in some psychosis studies may, in part, be due to the uncontrolled inclusion of individuals with a history of childhood trauma. Moreover, traumatic experiences in childhood may play an important role in brain morphology in FEP, relatively independent of psychotic symptoms.

The literature is replete with research indicating associations between trauma and neuroanatomical variables, irrespective of diagnosis. A meta-analysis has confirmed that a diagnosis of PTSD is associated with decreased hippocampal and left amygdalar volumes, while also revealing a similar influence of trauma in the absence of PTSD. In a BPD sample, volume differences between controls and those with BPD were only found when the BPD group also had a history of childhood abuse. Smaller hippocampal volumes have been observed in adult women with major depressive disorder with a history of childhood abuse.

Our results, when considered with an earlier neurocognitive article, suggest that specific neurocognitive deficits and neuroanatomical abnormalities observed in psychosis may at least in part be a consequence of childhood trauma. Difficulties arise when comparing the studies because of variations in illness trajectory and diagnostic groups as the previous neurocognitive articles predominantly focus on samples with chronic difficulties. However, the combined findings, irrespective of study variations, strengthen the proposition that childhood trauma is exerting an effect.

If reported structural abnormalities are sometimes a product of the experience of early childhood trauma and the inclusion of traumatized individuals in study samples, then we would expect to find some similar structural abnormalities in UHR and FEP groups. While one study suggests that structural changes occur only after the onset of psychotic symptoms, this is not supported by other research reporting hippocampal reductions in a UHR and first-episode groups as compared with controls.

This study is limited by a number of factors. The small sample size reduces the statistical power of the study but is however comparable to other FEP MRI studies. In addition, from the observations reported here, while associations can be determined, causality cannot be inferred.

A number of additional factors that were not controlled for in the analyses may also play an important role in brain morphology in psychosis. Diagnostic category may be important as research suggests that while the amygdala may facilitate hippocampal-dependant memory processes in BPD, it may impair these same processes in schizophrenia. Younger age of traumatic experience may also be important because the consequences of trauma appear more detrimental at an earlier stage of brain development.
This study provides evidence that childhood trauma is a potentially important explanatory variable for neuroanatomical observations in FEP. However, many questions remain regarding the exact nature of the relationship. The use of longitudinal studies with UHR and traumatized groups offers a promising method of disentangling the conflicting morphometric findings in psychosis populations.

Funding

The study was partly funded by the Research & Development Office for Northern Ireland.

Acknowledgments

The authors have declared that there are no conflicts of interest in relation to the subject of this study.

References


