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Traumatic brain injury in individuals at clinical high risk for psychosis

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ABSTRACT

Background: Recent research suggests that a traumatic brain injury (TBI) can significantly increase the risk of later development of psychosis. However, it is unknown whether people at clinical high risk (CHR) of psychosis have experienced TBI at higher rates, compared to otherwise healthy individuals. This study evaluated the prevalence of mild TBI, whether it was related to past trauma and the relationship of mild TBI to later transition to psychosis.
Methods: Seven-hundred forty-seven CHR and 278 healthy controls (HC) were assessed on past history of mild TBI, age at first and last injury, severity of worst injury and number of injuries using the Traumatic Brain Injury Interview. Attenuated psychotic symptoms were assessed with the Scale of Psychosis-risk Symptoms. IQ was estimated using the Wechsler Abbreviated Scale of Intelligence and past trauma and bullying were recorded using the Childhood Trauma and Abuse Scale.
Results: CHR participants experienced a mild TBI more often than the HC group. CHR participants who had experienced a mild TBI reported greater total trauma and bullying scores than those who had not, and those who experienced a mild TBI and later made the transition to psychosis were significantly younger at the age at first and most recent injury than those who did not.
Conclusion: A history of mild TBI is more frequently observed in CHR individuals than in HC. Inclusion or study of CHR youth with more severe TBI may provide additional insights on the relationship between TBI and later transition to psychosis in CHR individuals.

1. Introduction

A traumatic brain injury (TBI) is characterized as an alteration in brain functions caused by an external force (Reis et al., 2015). A TBI is known to lead to a variety of psychiatric problems in as high as one third of those who suffer a TBI, such as mood and anxiety disorders, personality changes, as well as impairments in Intelligence Quotient (IQ) and neurocognition (Deb et al., 1999; Kim et al., 2007; Konigs et al., 2015; Masel and DeWitt, 2010; Nicholl and LaFrance, 2009). More recent work suggests that a TBI may also be a risk factor for psychosis. In particular, a recent meta-analysis reported that a TBI significantly increased the risk of later development of schizophrenia by approximately 60% (Molloy et al., 2011). However, estimates of increased risk vary widely according to sample selection, with risk estimates typically elevated and more likely to be inaccurate in psychotic samples where TBI history is taken retrospectively, relative to estimates drawn from patients with a TBI who later develop psychosis (Batty et al., 2013). Moreover, it is difficult to determine whether a TBI leads to psychosis or whether an individual was already on a course towards psychosis prior to the injury (David and Prince, 2005). Interpretation is further complicated by the retrospective manner in which data on TBI were collected in schizophrenia samples (Molloy et al., 2011).

The risk of psychosis following a TBI is highest in individuals with a family history of the disorder (Kim, 2008) suggesting that the

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relationship of TBI to schizophrenia may involve a combination of a genetic predisposition to psychosis and environmental insult to the brain (AbdelMalik et al., 2003). Even in those at risk for psychosis, those with a family history reportedly experienced a greater number of lifetime head injuries compared to a healthy control group as evaluated with the Traumatic Brain Injury Interview, a 24 question clinician-rated scale (Stowkowy and Addington, 2013). Moreover, people at CHR of psychosis reported higher rates of trauma and bullying compared to healthy controls (Addington et al., 2013; Bechdolf et al., 2010) and it has been found that adolescents with a history of TBI are vulnerable to psychological and behavioral harms that co-occur with their history of TBI (Ilie et al., 2014).

However, it is unknown whether CHR individuals who had experienced a mild TBI also report significantly greater rates of trauma and bullying. This is an important consideration, as approximately 35% of people at CHR of psychosis will go on to develop a full blown psychotic disorder (Fusar-Poli et al., 2012). Thus this population offers a window of opportunity to evaluate the presence of TBI in people who have a greater risk of developing psychosis compared to the general population. These individuals present with attenuated psychotic symptoms, brief intermittent psychotic symptoms, or have a genetic risk for the disorder and a recent decline in functioning (McGlashan et al., 2010). The CHR cohort offers a unique opportunity to examine the prevalence of TBI and its impact on IQ prior to the onset of psychosis in people with a greater probability of developing a psychotic disorder relative to the general population, but who do not have a full blown psychotic disorder as in the retrospective research described above. However, TBI is typically an exclusion criteria in studies of clinical high risk. In the North American Prodromal Longitudinal Study (NAPLS 2) there were clear exclusion criteria with respect to moderate and severe TBI, typical of other studies (Brewer et al., 2005). The aims of the current study were to evaluate, in a large sample of youth at CHR of psychosis the prevalence of mild TBI, whether it was related to positive symptoms, differences in IQ, past experiences of trauma and bullying, and the relationship of mild TBI to later transition to psychosis.

2. Materials and methods

2.1. Participants

All participants were recruited as part of the eight-site NAPLS 2 study (Addington et al., 2012), which was established to investigate predictors and mechanisms of transition to psychosis. As described in Addington et al. (2012) all participants are help-seekers and were responding to similar recruitment strategies across sites. All participants were screened for TBI at the initial screening visit. This paper reports on the 747 CHR participants that completed the Traumatic Brain Injury questionnaire (AbdelMalik et al., 2003) at the baseline assessment. All CHR participants were required to meet the Criteria of Psychosis-risk Syndromes (COPS) using the Structured Interview for Psychosis-risk Syndromes (SIPS) (McGlashan et al., 2010). Participants were excluded if they met criteria for any current or lifetime axis I psychotic disorder, IQ <70 based on the WASI (Wechsler, 1999), past or current history of central nervous system disorder or DSM-IV criteria for current substance dependence disorder. HC participants were excluded if they had a first degree relative with a current or past psychotic disorder or any other disorder involving psychotic symptoms, met criteria for any prodromal syndrome, any current or past psychotic disorder or a Cluster A personality disorder diagnosis, or were currently using psychotropic medication. A more detailed description of participant details is provided elsewhere (Addington et al., 2012).

Informed consent was obtained from those who met criteria and were judged fully competent to give consent. Parental consent was obtained from parents/guardians of participants who were under age 16. The study was approved by the Institutional Review Boards of all eight NAPLS-2 sites.

2.2. Measures

The SIPS and the Scale of Psychosis-risk Symptoms (SOPS) (McGlashan et al., 2010) were used to assess criteria for a prodromal syndrome and severity of attenuated positive symptoms and negative symptoms.

IQ was assessed with the block design and vocabulary subtests of the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1987).

Trauma and bullying was assessed using the Childhood Trauma and Abuse Scale (Janssen et al., 2004). This measure is a semi-structured interview in which the interviewer inquires about trauma and abuse before the age of 16 including any emotional, physical, psychological or sexual abuse they may have experienced. Participants are also asked about any psychological or physical bullying.

The Family Interview for Genetic Studies (FIGS) (Maxwell, 1996) was used to determine the presence of a psychotic disorder in a first degree relative.

The Traumatic Brain Injury (TBI) Interview (AbdelMalik et al., 2003) was used to assess previous history of head injury. This interview captures the age at the first TBI, age at most recent TBI, number of TBIs reported, and the rating of the most severe TBI. Ratings of the most severe TBI were based on a scale of 1 (No head injury) to 8 (head injury with loss of consciousness/coma lasting 6 h or more, and/or skull fracture, and/or positive findings on head CT/MRI). Participants were excluded from NAPLS 2 if they experienced a moderate to severe TBI (i.e. ratings of 7 and above), any head injury that resulted in >30 min loss of consciousness. Participants were also excluded if they had sustained 3 or more, mild TBI with loss of consciousness of >5 min, their symptoms persisted for >2 months or the TBI had occurred in the 2 months prior to recruitment.

2.3. Statistical analysis

Chi-square analyses for categorical variables and t-tests for continuous variables were used to compare CHR and HC groups on demographic variables. The age at first and most recent TBI, severity of the most recent TBI, and number of TBIs variables were non-normally distributed; therefore, the non-parametric Mann Whitney *U* test was used for analysis involving these variables. Univariate analysis of variance was used to compare CHR and controls with and without a history of mild TBI on IQ. Chi Square was used to compare CHR and controls with and without a history of mild TBI on sex, and in CHR with and without a history of mild TBI on family history of psychosis. *T*-tests were used to compare CHR with and without a history of mild TBI on SOPS symptom severity. Kruskal-Wallis was used to compare CHR and controls with and without a history of mild TBI on trauma and bullying scores. Statistical analyses were conducted using SPSS 22.

2.4. Procedures

All eight sites (Emory University, Harvard University, University of Calgary, University of California at Los Angeles, University of California at San Diego, University of North Carolina at Chapel Hill, Yale University, and Zucker Hillside Hospital) recruited CHR individuals and HC participants. Raters were experienced research clinicians who demonstrated adequate reliability at routine reliability checks. Gold standard post-training agreement on the critical threshold for determining initial eligibility and subsequent transition status based on the SIPS was excellent (kappa = 0.90). The Principal Investigator or clinical psychiatrist or psychologist at each site conducted a comprehensive clinical assessment to determine if entry criteria were met. JA chaired weekly conference calls to review criteria for all individuals admitted to the study. Clinical assessments that included the SOPS were conducted at baseline. Assessments including the IQ, Childhood Trauma and Abuse and Traumatic Brain Injury (TBI) Interview were conducted at baseline

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