



Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

The traumatic experience of first-episode psychosis: A systematic review and meta-analysis

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ARTICLE INFO

Article history:

Received 9 December 2016

Received in revised form 23 January 2017

Accepted 26 January 2017

Available online xxxx

Keywords:

First-episode psychosis

Trauma

Post-traumatic stress disorder

ABSTRACT

Introduction: A psychotic episode may be sufficiently traumatic to induce symptoms of post-traumatic stress disorder (PTSD), which could impact outcomes in first-episode psychosis (FEP). The objectives of this systematic review and meta-analysis were to estimate the prevalence of PTSD symptoms in relation to psychosis in FEP and to identify risk factors for the development of PTSD symptoms.

Methods: We searched electronic databases and conducted manual searching of reference lists and tables of contents to identify relevant studies. Quantitative studies were included if the population was experiencing FEP and if PTSD was measured in relation to psychosis. Prevalence of PTSD symptoms and diagnoses were meta-analyzed using a random effects model. Potential risk factors for PTSD symptoms were summarized qualitatively.

Results: Thirteen studies were included. Eight studies assessed PTSD symptoms, three studies assessed full PTSD, and two studies assessed both. The pooled prevalence of PTSD symptoms was 42% (95% CI 30%–55%), and the pooled prevalence of a PTSD diagnosis was 30% (95% CI 21%–40%). Exploratory subgroup analyses suggest that prevalence may be higher in affective psychosis and inpatient samples. Evidence from included studies implicate depression and anxiety as potential risk factors for PTSD symptoms.

Conclusions: Approximately one in two people experience PTSD symptoms and one in three experience full PTSD following a first psychotic episode. Evidence-based interventions to treat PTSD symptoms in the context of FEP are needed to address this burden and improve outcomes after the first psychotic episode. Further studies are needed to clarify the associated risk factors.

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1. Introduction

The experience of a psychotic episode has been described as traumatic (Birchwood, 2003; Dunkley et al., 2015). Psychotic symptoms, such as delusions and hallucinations, can cause intense fear and distress (Shaner and Eth, 1989) and some people may experience coercive treatments such as involuntary hospitalization, seclusion, restraints, or forced treatment (Paksarian et al., 2014). Even the experience of hospitalization to an acute psychiatric ward has been noted as upsetting (Dunkley et al., 2015).

According to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5), a traumatic event is defined as “exposure to actual or threatened death, serious injury, or sexual violence”, and exposure to such an event is required for a diagnosis of post-traumatic stress disorder (PTSD; American Psychiatric Association, 2013). Although psychosis and associated treatment does not technically satisfy

this criterion, the subjective impact of psychosis may be sufficiently traumatic to result in symptoms of PTSD. Consequently, the primary symptoms of PTSD—re-experiencing the trauma, avoidance of trauma-related stimuli, and hyperarousal—have been observed in people with psychosis in relation to their experience of symptoms or hospitalization (Shaner and Eth, 1989).

PTSD in people with severe mental illness has been associated with psychiatric symptom severity and comorbid conditions (Mueser et al., 2004a, 2004b; Minsky et al., 2015; Ng et al., 2016), greater impairment of functioning (Minsky et al., 2015; Ng et al., 2016; Seow et al., 2016), and lower engagement and satisfaction with mental health services (Minsky et al., 2015; Switzer et al., 1999). It has been hypothesized that PTSD symptoms related to psychosis may impact treatment adherence through avoidance of trauma-related stimuli (Mueser and Rosenberg, 2003). In the context of first-episode psychosis (FEP), it has been suggested that negative experiences with health services at first contact initiate patients on a trajectory that may impact long-term outcomes (Anderson et al., 2010). Considering the importance of early treatment in FEP for reducing the consequences of untreated psychosis (Marshall et al., 2005; Perkins et al., 2005), and the potential impact of treatment experiences on adherence and health care utilization

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(Minsky et al., 2015; Mueser and Rosenberg, 2003), unrecognized PTSD symptoms may have a particularly detrimental impact on recovery in this population.

Many studies investigating PTSD symptoms related to psychosis report mixed first- and multi-episode populations, and prevalence estimates vary widely, ranging from 11% to 70% (Berry et al., 2013). Although many factors are likely to influence varying prevalence estimates—including the timing of PTSD assessment, the instrument used, geographic location, or treatment setting—we hypothesize that the chronicity of the sample may impact prevalence estimates (Berry et al., 2013), as the novelty of the first episode of psychosis may be more traumatic than recurrent episodes (Mueser and Rosenberg, 2003). Our primary objective was to systematically review the literature to estimate the prevalence of PTSD symptoms after the first episode of psychosis. Our secondary objective was to investigate potential risk factors for PTSD symptoms to determine whether there are subgroups of patients particularly vulnerable to experiencing PTSD symptoms after a first episode of psychosis.

2. Methods

2.1. Search strategy

We searched the following electronic databases (1980–2016, inclusive): MEDLINE-Ovid, EMBASE-Ovid, PsycINFO-Ovid, Cochrane Library, Web of Science, the Published International Literature on Traumatic Stress (PILOTS) database, Theses Canada Portal, and the Networked Digital Library of Theses and Dissertations (NDLTD). No language restrictions were imposed. MEDLINE search terms (Supplementary Appendix A) were adapted to other databases. The database searches were updated regularly, with the last update occurring July 30, 2016.

We used forward and backward citation searching and manual searching of tables of contents (*British Journal of Clinical Psychology*, *Journal of Consulting and Clinical Psychiatry*, *Early Intervention in Psychiatry*, *Social Psychiatry and Psychiatric Epidemiology*, and *Journal of Traumatic Stress*). We contacted authors of abstracts or unpublished studies to determine whether the studies had subsequently been published in a peer-reviewed journal. The search strategy was developed in consultation with a medical librarian.

2.2. Study selection and data extraction

Two independent reviewers screened titles, abstracts, and full-texts, and completed data extraction. Studies were included if: (i) the population was FEP or presented stratified data for first- and multi-episode cases; (ii) PTSD symptoms were measured in reference to psychosis or associated treatment experiences; and (iii) the study design was quantitative. We assessed study quality using an adapted Newcastle-Ottawa Scale (Table 1; Wells et al., 2013). The representativeness of sample domain was adapted to include options for a population-based sample, mixed inpatient/outpatient sample (unrestricted), and restricted inpatient sample. Ascertainment of exposure (i.e., psychosis) was adapted to include clinical interview, clinical chart diagnosis, and self-report. Ascertainment of outcome (i.e., PTSD symptoms) was adapted to include a clinical diagnosis and screening tool. Discrepancies between reviewers were discussed and resolved by consensus. We contacted corresponding authors when methodological questions arose or if more detailed data were required for analysis.

2.3. Meta-analysis

We divided studies into two groups for the meta-analysis based on whether studies used self-report scales to assess PTSD symptoms or clinical interviews to diagnose PTSD, irrespective of DSM criteria for a traumatic event. Studies reporting both PTSD symptom and diagnosis prevalence were included in both analyses. Proportions of participants

meeting scale cut-offs for clinically relevant PTSD symptoms, or meeting diagnostic criteria for PTSD, were meta-analyzed to obtain pooled prevalence estimates and 95% confidence intervals (CI). We used the Freeman-Tukey double arcsine transformation (Freeman and Tukey, 1950) within a random effects model to account for methodological and clinical heterogeneity, including sample characteristics, PTSD instruments, and timing of assessments.

We used post-hoc exploratory subgroup analyses to examine the influence of factors hypothesized to affect PTSD symptom prevalence (Berry et al., 2013). First, we meta-analyzed PTSD symptom prevalence in subgroups containing affective versus non-affective psychosis using two strategies—by contacting study authors to obtain stratified data, and by dividing studies based on the median percentage of non-affective psychosis. We meta-analyzed the prevalence of PTSD symptoms and diagnoses in studies with unrestricted inpatient/outpatient versus restricted inpatient samples. We further explored these factors by removing studies from the meta-analysis that contain both affective samples (i.e., below the median percentage of non-affective psychosis) and restricted inpatient samples. We also conducted subgroup analysis to investigate regional differences in PTSD symptom prevalence. We used sensitivity analyses to examine the influence of individual studies and quality criteria on pooled prevalence estimates. We assessed statistical heterogeneity using the I^2 statistic with cut-off values of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity (Higgins et al., 2003). We evaluated publication bias using a funnel plot for proportions and visually inspected the plots for asymmetry of study proportions around the average (Spiegelhalter, 2005). Publication bias was assessed only when there were at least ten studies in the meta-analysis (Higgins and Green, 2011).

Meta-analyses were conducted in Stata 13.0 using the *metaprop* command (Nyaga et al., 2014) and funnel plots were constructed in SAS 9.4. Potential risk factors for PTSD (symptoms or a diagnosis) were summarized qualitatively.

3. Results

The database search retrieved 1186 studies and 39 were reviewed at the full-text stage (Fig. 1). Thirteen studies met the inclusion criteria and reported prevalence of PTSD symptoms ($n = 10$) (Abdelghaffar et al., 2016; Bendall et al., 2012; Bernard et al., 2006; Jackson et al., 2004; Jackson et al., 2009; McGorry et al., 1991; Mueser et al., 2010; Pietruch et al., 2012; Stubbins, 2014; Turner et al., 2013) and/or diagnoses ($n = 5$) (Abdelghaffar et al., 2016; Brunet et al., 2012; Mueser et al., 2010; Sin et al., 2010; Tarrier et al., 2007). Nine studies were included in the qualitative synthesis of factors associated with PTSD symptoms/diagnoses (Fig. 1). Study characteristics are summarized in Table 2.

Nine studies described aspects of psychosis and treatment participants found to be traumatic. These experiences included psychotic symptoms (31% to 75% of patients), hospitalization/treatment (22% to 46% of patients), and experiences such as behaviour when ill, paranoia and mental disturbance, police involvement, fear of other patients, and negative staff attitudes (Table 2).

None of the studies satisfied all quality criteria domains (Table 1). Problems included high non-participation rates and/or lack of a description of participation ($n = 11$), no adjustment for important confounding factors ($n = 11$), no adjustment for additional confounding factors ($n = 9$), and non-representativeness of samples ($n = 4$).

3.1. Meta-analysis of PTSD prevalence

Across eight studies (pooled $n = 398$), 42% (95% CI = 30%–55%, $I^2 = 83.8\%$) of people with FEP displayed clinically relevant PTSD symptoms related to psychosis up to 2.5 years following the first-episode (Fig. 2). Across four studies (pooled $n = 204$), the prevalence of full PTSD was 30% (95% CI = 21%–40%, $I^2 = 53.9\%$) within two years of the first-episode (Fig. 2). The funnel plot for PTSD symptoms displayed no evidence

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