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Review

The prevalence and moderators of clinical pain in people with schizophrenia: A systematic review and large scale meta-analysis

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ABSTRACT

Background: People with schizophrenia frequently have physical comorbidities that can cause pain. Experimental studies report reduced pain sensitivity among schizophrenia patients, but it remains unclear if clinically relevant pain is less prevalent in schizophrenia.
Method: We systematically searched major electronic databases from inception till 03/2014. Articles were included that reported the prevalence of clinical pain in people with schizophrenia. Two independent authors conducted searches, completed methodological quality assessment and extracted data. A random effects relative risks (RR) meta-analysis was conducted to determine the prevalence of all-cause and specific pain in schizophrenia, and the relative prevalence compared to the general population, and to assess moderators.
Results: Altogether, 14 studies were included encompassing 242,703 individuals with schizophrenia (30.2–55.8 years) and 4,259,221 controls. Different types of pain were considered. The overall pooled prevalence of clinical pain in people with schizophrenia was 34.7% (95% CI = 23.6–46.6). In the comparative analysis involving 7 studies with controls, the RR was 0.99 (95% CI = 0.83–1.19). The pooled prevalence of headache among 94,043 individuals with schizophrenia was 29.9% (95% CI = 3–69%) and the RR compared to 4,248,284 controls was 1.32 (95% CI = 0.85–2.07). In moderator analyses, neither age, sex, study quality or pain assessment method influenced pain prevalence.
Conclusion: Clinical pain affects a third of people with schizophrenia and levels are similar with age- and sex-comparable controls. Future research is needed to determine if similar clinical pain prevalences in schizophrenia occur despite having more painful conditions, resulting from under-reporting, higher pain thresholds or lower help seeking behaviours.

1. Introduction

Pain has a deleterious impact upon an individual's health and quality of life. Chronic painful conditions, such as low back pain (LBP) are a leading cause of global burden accounting for a substantial amount of years lived with disability (Murray et al., 2013). A considerable amount of research established that pain is strongly associated with depressive symptoms (Katon et al., 2007; Means-Christensen et al., 2008), yet research considering the association with severe mental illness (SMI) is less clear. Recently, a meta-analysis involving over 12 million people found that people with bipolar disorder are more likely to experience pain than those without bipolar disorder in the general population (relative risk 2.14; 95% CI = 1.67–2.75, Stubbs et. al, in press). However, to date little attention has been given to clinical pain among people with schizophrenia. This requires consideration, as people with schizophrenia are at an increased risk of experiencing multiple physical comorbidities that can cause pain (Leucht et al., 2007; Mitchell et al., 2009; De Hert et al., 2011a, 2011b). Clinical pain is naturally occurring and is not elicited experimentally or through a medical procedure (e.g., lumbar puncture) and is important because it often drives people to seek medical help and may underlie a potential serious medical ailment (Scherder et al., 2003; Engels et al., 2014). Previous research has demonstrated that people with schizophrenia are less likely to be aware of co-occurring physical comorbidities and are less likely to

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receive subsequent medical treatment (Lord et al., 2010). It remains unclear if this observation extends to clinical pain.

For many years, there have been reports that under experimental conditions, people with schizophrenia have reduced pain sensitivity compared to the general population (Bleuler, 1951; Potvin and Marchand, 2008). However, studies measuring clinical pain have yielded conflicting results. For instance, in a study involving over 2400 people, Strassnig et al. (2003) found that individuals with schizophrenia reported a higher severity of bodily pain than members of the general population. In addition, previous research has demonstrated that most people with schizophrenia who are in pain do not report it (Kuritzsky et al., 1999) and the majority do not get the necessary treatment for their pain (Watson et al., 1981; De Almedia et al., 2013). Recently, Engels et al. (2014) conducted a narrative systematic review and report that people with schizophrenia only appear to have a reduced pain prevalence compared to healthy controls when studies are considered in which pain is stimulated by a medical procedure (e.g., lumbar puncture). While this review is helpful, the authors did not conduct a meta-analysis and they mixed together results from studies of clinically occurring pain and those that stimulated pain via medical procedures (e.g., lumbar acupuncture). Therefore, the overall prevalence of clinical pain in schizophrenia is not known. In addition, it is still unclear if people with schizophrenia have lower levels of clinical pain than members of the general population reported under the same conditions. A formal meta-analysis is required to answer these questions. Further, it remains unclear which factors may influence the prevalence of clinical pain in schizophrenia. For instance, increasing age and female sex have been implicated in the general pain literature (AGS, 2009), but it remains unclear if this extends to people with schizophrenia. In addition, study quality can influence the prevalence of pain, and a moderator analysis is required to investigate the impact of these factors on the prevalence of clinical pain in schizophrenia.

In recognition of the potential for pain to be problematic and potentially under recognised in people with schizophrenia, the study had the following three aims: 1) to establish the pooled prevalence of all-cause and specific-cause clinical pain in people with schizophrenia, 2) to compare the prevalence of clinical pain in people with schizophrenia with that in age- and sex-matched general population comparison groups, and 3) to identify potential moderators of clinical pain in people with schizophrenia.

2. Method

This systematic review was conducted in accordance with the MOOSE guidelines (Stroup et al., 2000) and in line with the PRISMA statement (Moher et al., 2009) following a predetermined protocol.

2.1. Inclusion and exclusion criteria

Studies were eligible that fulfilled the following criteria: 1) Included participants with schizophrenia, diagnosed according to diagnostic criteria (e.g., DSM IV, APA, 2000 or ICD 10, WHO, 1993) either prospectively or retrospectively through medical record review. If we encountered studies in mixed samples with schizoaffective disorder or psychosis, we attempted to extrapolate the variables of interest for people with schizophrenia. If this was not possible, we contacted the research groups to ascertain this information and if we did not receive a response, we included the study only if >80% had a diagnosis of schizophrenia. 2) Reported the prevalence of clinical pain (of any type or location) with or without a healthy comparison group that did not have a mental illness, referred to as the comparison group. We categorised the type of clinical pain where possible according to body location and duration (current pain was that for which the duration was not stated and chronic pain was lasting >3 months).

We excluded studies that reported the prevalence of non-clinical pain, i.e., stimulated by a medical procedure (e.g., lumbar puncture) or under experimental conditions. We also excluded studies that reported pain as an adverse event of a drug trial (e.g., headache) or reported the prevalence of schizophrenia in a biased sample of patients who all had pain. When we encountered studies that assessed pain in a sample with a continuous measure (e.g., SF 36 bodily pain scale), but did not provide a cutoff to determine the prevalence of pain, we contacted the authors up to two times to obtain this categorical information. If we were not able to ascertain the prevalence of pain, the study was excluded. We did not place any language restrictions upon our searches. When we encountered studies reporting data from the same sample at different time points, we used the most recent data and/or the largest data set.

2.2. Information sources and searches

Two independent reviewers searched Academic Search Premier, MEDLINE, Psychology and Behavioral Sciences Collection, PsycINFO, SPORTDiscus, CINAHL Plus and Pubmed from inception until March 2014. We used the key words 'schizophrenia' or 'schiz*' or 'psychosis' and 'pain*'. A third reviewer conducted additional searches to ensure completeness. In addition, the reference lists of all eligible articles and recent systematic reviews of pain in schizophrenia were screened to assess eligibility of additional studies. Primary/corresponding authors of research groups were contacted where necessary.

2.3. Data extraction

Two authors extracted data using a predetermined form. The data collected from each article included: study design, geographical location, details of schizophrenia participants (mean age, % males), diagnosis method, details of medications and chronicity of illness, and comparison group participant characteristics (mean age, % males). We extracted the prevalence of pain in people with schizophrenia and comparison groups where available. In addition we recorded details of the pain assessment including the method, site, duration, severity and interference of pain with daily activities.

2.4. Methodological quality assessment

Two authors completed methodological quality assessment of included articles using the Newcastle Ottawa Scale (NOS; Wells et al., 2010). Due to the paucity of data, we included studies without a comparison group and considered these as cross-sectional case control studies for methodological assessment in line with a recent review (Stubbs et. al, in press). Studies were given a NOS score ranging from 0 to 9, with a score of 5 or greater being indicative of satisfactory methodological quality. We anticipated that studies without a comparison group would score below this threshold and present their results with due consideration. In addition, in order to examine the influence of methodological quality upon the prevalence rates, we conducted a regression analysis coding results as satisfactory (NOS score >5) and not satisfactory (NOS 0–4).

2.5. Meta-analysis

First, we pooled all-cause and specific-cause prevalence results meta-analytically (Aim 1). Due to the anticipated heterogeneity we pooled individual study data using DerSimonian–Laird proportion meta-analysis (DerSimonian and Laird, 1986) with StatsDirect. Second, we calculated the relative risk to investigate the differences in pain between individuals with schizophrenia and members of the general population (Aim 2). Whenever possible, we conducted subgroup analysis to investigate the prevalence of pain according to the sub-groups of pain classification. In order to assess for heterogeneity we calculated Cochran's Q statistic for each analysis (Higgins et al., 2003). Third, we investigated the influence of moderators on the observed