Α	review of	factors	associated	with	severe	violence	in so	chizoph	renia
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Abstract

Background: There is a modest but consistent association between violence and schizophrenia. The consequences of serious violence are catastrophic for the victims, as well as the patients themselves and the community. Any knowledge that would help to prevent acts of serious violence would be of considerable value for the individual and the society. **Aim:**To identify external and clinical risk factors for serious violence in schizophrenia, in addition to considering the strength of the association between the factors assessed and severe violence.

Method: This was accomplished by a literature survey in which 102 relevant papers were identified that were published during the past 20 years. Forty-four papers were assessed for eligibility. In all, 27 studies including clinical or cognitive variables were reviewed systematically. An effect size was reported where an odds ratio (OR) could be identified or calculated from available data. Five external factors and six clinical domains were evaluated. Results: Substance abuse is robustly linking schizophrenia and violence. Among the clinical factors, insight, impulsivity, psychopathy, motor speed and a global measure of cognition are the factors with the strongest empirical evidence for an association with severe violence. Conclusion: This is the first systematic review of risk factors for severe violence in schizophrenia, in which a great number of clinical and external factors have been evaluated, and most of the clinical factors have been compared on effect size. The identified factors that represent an increased risk of violence in patients with schizophrenia should be included in risk assessments.

Key words:

Psychosis

Violence

Riskfactors

Clinical factors

Cognition

Homicide

Schizophrenia

Introduction

There is a modest but consistent association between violent behavior and schizophrenia (1-3). People with schizophrenia are clearly overrepresented among murderers, comprising 5-20% of all homicide offenders (4). This percentage is approximately 20 times higher than the estimated prevalence of psychotic illness in the general population (5). Approximately 4 in 10 of the homicides committed by people with psychosis occur prior to treatment (4). It has also been estimated that 6% of murderers suffer from schizophrenia (6, 7). The consequences of serious violence by patients with schizophrenia are catastrophic for the victims, their families, the patient themselves and the wider community. Hence any knowledge that would help to prevent even one such homicide would be of considerable value for the individual and the society.

There is limited knowledge about the aspects of schizophrenia that contribute to the potential for severe violence. If psychological risk factors can be more precisely identified, it is possible to develop better risk assessment instruments to be used in a clinical context.

In recent years, some systematic reviews and meta-analyses of the field have been conducted. The weakness of these is that most often very broad terms have been used, particularly when it comes to violence and diagnostic categories. Furthermore, few reviews have been done in which several psychological factors have been considered in one review or combined into one meta-analysis. The present review is an attempt to cover a wide range of risk factors, and with more refined criteria for violence and diagnosis(8).

Violence is a broad concept, including everything from verbal threats and hostility to homicide. Serious aggression may have associations to different psychological characteristics than less serious aggression (9). The lack of clear operationalized definitions of the term *violence* used in different studies has led to mixed results, thereby confounding efforts to summarize reviews in clear conclusions concerning which factors are related to violence (10). In this review we have strived to limit the search to severe violence, defined as homicide or other serious physical violent crime, corresponding to an assault resulting in serious injury or sexual assault.

Additionally, the diagnostic categories of the individuals examined have not been specified in some of the studies. We have reviewed these studies in cases in which relevant clinical factors are included. However, we have conferred the greatest weight to those

reports where the study sample has been limited to schizophrenia.

The purpose of this review is to identify risk factors for serious violence in schizophrenia, as well as to consider the strength of the empirical evidence of associations between the two factors. This is accomplished by a review of the relevant studies that emerge through a literature search. In those papers where it has been possible to identify the strength of the association between a specific factor and violence, the effect size (odds ratio; OR) is presented.

Methods

Study selection

We aimed to identify all studies available in which the association between external and psychological factors and severe violence in schizophrenia had been empirically addressed. Relevant reports were identified by a literature survey using the search terms "schizophrenia" or "psychosis," "violence" or "homicide," "prediction" or "association," "cognition" or "neurocognition" or "social cognition". All the terms were combined in separate surveys. A database search was performed on PubMed, PsycINFO and Embase. We specified the date of the search criteria to the last 20 years, i.e. 1997-2017. In total, 1474 articles were identified through the database search (Figure 1). Moreover, the reference lists of articles found during these search procedures were scanned by hand to identify additional studies, with 8 relevant publications coming to our attention in other ways. A total of 102 records were screened in full text after duplicates were removed and abstracts screened for 1427 papers. Forty-four articles were assessed for eligibility.

The review was split into 2 domains: external and clinical factors. Clinical factors consisted of symptoms and cognition.

Quantitative meta-analysis has become the most common approach for assessing the overall effects in multiple studies that have examined the same issue. In the present review, a meta-analytic approach was not deemed suitable because of the heterogeneity in samples, design, instruments and measures, and because sufficient data for a meta-analysis were not reported in all studies.

To a certain extent, what we have been doing in order to remedy the lack of a meta-

analysis is to present effect sizes for specific clinical domains in ORs in Figure 2. Some of these ORs are based on individual reports, others on meta-analyses. In studies in which associations were reported as continuous variables, log-transformed ORs were calculated from Cohen's d (2).

Figure 1 here

Inclusion criteria

Studies were included if they assessed the association between risk factors and severe violence in patients within the schizophrenia spectrum according to the DSM III/IV or ICD 9/10 criteria. Comparisons between violent schizophrenia patients and non-violent schizophrenia patients have been made. In the population survey studies included in this review, the association between violence and a risk factor has been evaluated.

Reviews were only conducted on risk factors examined in 3 or more studies. This approach was adopted to improve validity of risk estimates, and to restrict the number of different risk factors reported (2). Seventeen papers formed the basis for the review of external factors. Twenty-seven reports were included in the qualitative review on the association between clinical characteristics and violence (see Table 1), whereas the effect sizes presented in Figure 2 were based on 11 separate papers.

The papers were assessed against the following methodological issues: (a) Is the research design adequate and relevant? (b) Is there a sufficient number of participants? (c) Were the concepts of violence and the psychological risk factors adequately defined?

Results

External factors

Substance abuse: Substance abuse in schizophrenia is associated with the most severe form of violence (7, 11). In a meta-analysis of violence in first-episode psychosis (12) it was found that substance use was associated with violence of any severity with an OR of 2.33, and with an effect size of 2.74 after the first episode of psychosis. In a prospective study (13) it was

showed that the model that best predicted assault in schizophrenia patients included alcohol abuse (OR of 3.55). In a Swedish sample it was found an OR of 4.3 for drug or alcohol misuse prior to admission in psychosis patients who committed homicide after discharge when compared to patients who had no violent convictions (14). Nielssen et al. (15) found that 73% of those psychotic people charged with homicide reported substance misuse. Worth noting is that only 35% reported to have been intoxicated at the time of the offense. Finally, in a comprehensive review (2) a meta-regression analysis was used to identify risk domains of violence. When restricting the studies to those which measured severe violence, they calculated the OR for substance misuse to be 2.2.

Even though it has been argued that substance abuse is the main driver of violence in schizophrenia (7), and that there is almost no role for psychosis-specific factors, there is also data which shows that patients with schizophrenia without comorbid substance abuse do have an elevated risk of violence (16, 17). Furthermore, a Japanese study did not find an association between substance abuse and violence (18). Consequently, although substance abuse can explain much of the variance in relation to violence when schizophrenia patients with violence are compared with schizophrenia patients without violence, substance abuse does not explain it all.

Treatment

Phase of illness: Nielssen and Large (4, 12, 15) have shown that people in the first episode of psychosis are at greater risk of committing serious violence than those in subsequent episodes. In a review of violence in first-episode psychosis, they (12) showed that approximately one-third of patients in the first episode exhibited some violent behavior before initial treatment, and that approximately 16% committed an act of more serious violence. Notably, the factors associated with violence in first-episode psychosis are similar to the factors associated with violence in patients with established mental illness. In a meta-analysis of 10 studies (894 people) of homicide rates in first-episode psychosis, they showed that 38.5% of homicides occurred during the first episode of psychosis (4).

Duration of untreated psychosis (DUP): As an extension of the referenced knowledge about the first episode of psychosis, there is also some evidence that the duration of untreated

psychosis (DUP) is directly related to serious violence (9, 15, 18-20). This can be seen in the context of a neurotoxic effect of untreated psychosis (21).

Treatment compliance: In the meta-analysis of first-episode psychosis (12) three studies showed that involuntary treatment was strongly associated with violence in the period following the initiation of treatment. Also, non-adherence with treatment is associated with severe violence (2, 14).

Childhood abuse: Spidel et al. (22) examined early-onset psychosis patients, and found that those who were victims of child abuse were more likely to be violent in later life. A meta-analysis of violence in psychosis, in which 4 studies of physical abuse and 3 of sexual abuse during childhood were included, demonstrated that violence was associated with reported physical abuse (OR 2.2) and sexual abuse (OR 1.9).

Table 1 and Figure 2 here

Clinical factors

Many studies suggest that serious violence is associated with (positive) symptoms.

Hallucinations: Volavka et al.(23) found that auditory hallucinations were associated with violence, while Swanson et al. (24) reported that an increased risk of serious violence was strongly associated with hallucinatory behavior (Table 1, Figure 2). Nielssen et al. (15) found that in a sample of 88 psychotic patients who had committed homicide, auditory hallucinations giving rise to persecutory delusional beliefs were the most common symptoms. In a study by Lee et al. (5) 81% of the offenders of severe violence reported auditory hallucinations .

Delusional beliefs: Swanson et al. (24) reported that serious violence was associated with grandiosity (Figure 2). In a study of 74 patients with a psychotic illness who had committed a severe violent offense, 92% of them reported delusional beliefs at the time of the offense (5). Coid et al. (25) examined a total of 458 first-episode psychosis patients during a 2-year study period. When comparing a group of serious violent patients with a non-violent

subgroup, they found a strong relationship between serious violence and delusional content that implied a threat, such as delusions of being spied on, persecutory delusions, and delusions of conspiracy. Anger due to delusions was identified as a potential mediator for the delusional beliefs. Thus, they concluded that anger due to delusions is a key factor in explaining the relationship between violence and acute psychosis. But it might also be that a subset of delusional beliefs is causally linked to violence.

In a recent meta-analysis individual subject data from 7 population surveys were included (26). This is an examination of the association between severe violence and paranoid ideation among survey respondents. Paranoid ideation was strongly associated with any type of violence (OR 2.26), as well as severe violence defined as a victim being injured (OR 1.78). These findings correspond to the relationship between delusions and violence found in more recent clinical samples (25, 27). In a review of 15 studies on the relationship between paranoia and aggression in psychosis the findings were summarized by claiming that there is a mixed support for an association between paranoia and aggression in people with schizophrenia (28). When the study quality was taken into account, however, better quality studies tended to show a positive association between the two factors.

Insight: Arango et al. (29) found that violent inpatients with schizophrenia had less insight than non-violent patients. Lack of insight into psychotic symptoms was the best single predictor of violence. Verma et al. (20) also reported significantly poorer insight in first-episode violent psychosis patients compared to non-violent patients. Another study (30) showed that a lack of insight was associated with aggressive behavior in univariate analyses, but did not contribute to the prediction of aggressive behavior once scores for psychopathy and positive symptoms were entered into the model. Further, a Turkish study (31) demonstrated that violent patients exhibited worse clinical and cognitive insight than did non-violent schizophrenia patients. Lastly, Witt and associates (2) found a significant association between lack of insight and risk of violence in individuals diagnosed with psychosis when lack of insight was used as a dichotomous variable (Figure 2). When lack of insight was used as a continuous variable in three other studies, the association between violence and lack of insight turned out to be non-significant.

Impulsivity: Verma et al. (20) studied aggression in first-episode psychosis. They found that poor impulse control measured by PANSS was significantly elevated in patients with severe

violence (Figure 2). Contrary to the Verma study, Ekinci and Ekinci (31) did not find significant differences in the impulsivity scores of the violent and non-violent schizophrenia group. Nonetheless, they reported that a substantial portion of the group defined as violent had little or no history of violent behavior, which is a decisive limitation of the study. Bjørkly's (32) review identified only four studies that examined the association between impulsivity and violence in persons with psychosis. Bjørkly's assessment is that the evidence of a link between impulsivity and violence appear to be inconclusive concerning psychotic patients. A meta-analysis (2) concluded that there is a strong association between poor impulse control and risk of violence in individuals diagnosed with psychosis (Figure 2).

Psychopathy: In addition to substance abuse, psychopathy has been considered to be the factor that most robustly linking schizophrenia and violence.

In a cohort of Swedish offenders with schizophrenia, the relative risk for violent recidivism during a follow-up time (M= 51 months) among psychopaths was compared to non-psychopaths. A survival analysis revealed that psychopathy was strongly associated with violent recidivism (33). Among psychopaths, the violent recidivism rate was 48%, while among non-psychopaths the failure rate was 14%. The relative risk of violent recidivism among psychopaths was 1.67. Another study (30) reported that among people with schizophrenia living in the community, aggressive behavior was more strongly associated with high scores for psychopathy traits than with lack of insight. Spidel et al. (22) examined early-onset psychosis patients and found that higher scores on the psychopathy measure (SRP-II (34)) were linked with violence history. However, it did not significantly predict violence (Figure 2). A Japanese study (18) examined factors associated with violence among patients with schizophrenia prior to hospitalization. They argued that violence was strongly associated with elements of schizophrenia itself, rather than antisocial traits.

Witt et al. (2) pooled seven studies that included psychopathy scores in their metaanalysis (N=183 violent patients). Examining the association between psychopathy and violence, they reported a very high OR (Figure 2). They also examined the association between antisocial personality disorder (4 studies) and violence, and found an OR of 2.1. In a review paper (35) it was concluded that schizophrenia without any comorbidity confers an elevation of the risk for violence, and that the risk is considerably increased by comorbid antisocial personality disorder or psychopathy. Violence among adults with schizophrenia may follow at least two distinct pathways: one associated with premorbid conditions, including antisocial conduct, and another associated with the acute psychopathology of schizophrenia.

Cognition

Past studies have yielded mixed results regarding the significance of neurocognitive impairment as a risk factor for severe violence. Some recent examinations have supported such an association, and one study indicated that cognitive processes are valuable predictors of aggressive in-clinic incidents (36).

Barkataki et al. (37) compared neuropsychological performance in schizophrenia patients with severe violence and non-violent individuals with schizophrenia. The groups were rather small, 13 and 15 patients, respectively. The non-violent group performed significantly better than the violent group on two measures of executive functioning: perseverative errors on Wisconsin Card Sorting Test (WCST) (38) and processing on the Stroop Colour-Word task (39) (Figure 2). Silver et al. (40) compared schizophrenia patients with and without a history of violence, and a healthy control group was also included. A broad battery of neuropsychological tests was used, assessing attention, working memory, executive function and motor function, visual orientation and memory of faces and objects. Schizophrenia patients performed worse than healthy controls, although no significant differences were found between violent and non-violent schizophrenia patients. Harris et al. (9) examined first-episode psychosis patients with a comprehensive cognitive test battery. They found that errors of commission on a Continuous Performance Task, which is considered to be a measure of reduced behavioral inhibition, was significantly associated with serious aggression. Chung et al. (41) compared 51 male patients with schizophrenia who had committed homicide, with 50 male patients who had not committed homicide. No significant differences were found between the homicidal and non-homicidal groups on any of the four neuropsychological tests, nor on the intelligence scale. Yet, the aggression scores of the non-homicide schizophrenia group make it unclear whether these patients were completely non-violent; therefore, firm conclusions can hardly be drawn from this study.

O'Reilly et al. (42) examined whether neurocognition and social cognition predicted inpatient violence among patients with schizophrenia and schizo-affective disorder over a 12-month period. The total number of patients examined was 89, with 10 of them being violent. Cognition was assessed by the MATRICS Consensus Cognitive Battery (MCCB)(43). Violent patients performed significantly worse than non-violent patients on the MATRICS domains of processing speed (EZ d= 0.76), verbal learning (EZ d = 0.92), social cognition (EZ d= 1.14) and the total composite score (EZ d = 0.80) (Figure 2). The effect size of reasoning (executive function) was non-significant (d= 0.30). In total, these findings show a robust association between cognitive deficits and violence, accounting for 34% of the variance in violent incidents after controlling for age and gender during the follow-up period. The OR of 4.26 for the association between the MCCB composite score and violence is among the highest effect sizes in this review (Figure 2). Bulgari et al. (44) compared 50 violent schizophrenia spectrum patients and 37 non-violent patients, who were followed-up for 1 year Contrary to what was expected, the violent patient group performed better than the non-violent group on executive function and motor tasks. Better performance was linked to symptoms in the violent group, through an inverse correlation between cognitive performance and the severity of negative symptoms (Figure 2). Thus, it seems as an association between relatively superior motor speed performance and violence in schizophrenia patients may be partly determined by low levels of negative symptoms in comparison with non-violent controls.

There have been several meta-analyses conducted on the relationship between neurocognition and violence in psychosis. Note that some of them were done before the more recent studies, which found a significant association between violence and one or more cognitive factors (see above). One study (45) found no association between cognitive deficits and aggression in schizophrenia in their review. They concluded that violent patients perform better than non-violent patients on executive function and verbal skills. Their conclusion is based on six of the reviewed studies that indicated that patients with a history of aggressive behavior, compared with those with no history of violence, performed equally well or even better on executive function tests. However, three other studies in their review found that violent patients performed more poorly than non-violent or low violence patients. Naudts and Hodgins mainly attribute the inconsistent results to varying definitions of violence, differences in sample characteristics and diverse neuropsychological measures

in the studies examined. Most of the studies in the review of Naudts and Hodgins were published more than 20 years ago, and many of them assessed intellectual ability rather than cognitive function. Those studies in the review that were less than 20 years old, and included a broader battery of neuropsychological tests, have been reviewed separately in the current review.

In another review (2) it is concluded that none of the neuropsychological factors investigated were significantly associated with violent outcomes. However, it is worth noting that the factors that were examined exclusively involve intellectual capabilities. Moreover, Witt et al. (2) did not specify which studies were included in their review. They reported a pooled OR magnitude of 1.5 for the risk of severe violence in psychosis.

Reinhart and associates (46) conducted a meta-analytic review of the association between cognitive deficits and aggression in schizophrenia. Note that this is a review of aggression in general, not limited to severe violence. Twenty-nine research papers that related neurocognitive measurements to aggressive behavior in psychosis were reviewed, concluding that there is mounting evidence to suggest that cognitive functioning relates to an increase in the likelihood of aggression in schizophrenia. They calculated that impaired cognitive functioning explains approximately 2% of the variance. Still, this figure seems to apply to a broader psychosis group not limited to schizophrenia, in which cognitive deficits are more pervasive. Furthermore, Reinhart et al. (46) concluded that the most reliable way to assess the association between cognition and aggression is through a measure of global cognitive capacity. They reported the following effect sizes: OR 0.72 for insight, OR 0.61 for global cognition and OR 1.52 for motor functioning (in the direction contrary to prediction, i.e. better motor functioning correlates with an increased likelihood of aggression) (Figure 2). Reinhart et al. (2014) point out that the ability to reliably relate cognitive factors to aggression depends on data collection and methods.

Richard-Devantoy et al. (47) reviewed neurocognitive vulnerability to homicidal behavior in patients with schizophrenia. They included five studies that explored executive function in relation to homicide. In three of these studies, schizophrenia patients with a history of homicidal behavior performed more poorly than schizophrenia patients without such a history on several executive functions, including mental shifting, cognitive inhibition and verbal fluency. Two studies reported no such group differences (40, 48). Because there is so little information about the individual studies, and the authors provide scant

information about the basis for their conclusion, this review cannot be given considerable weight.

Discussion

Although the current review shows mixed findings for almost all of the external and clinical factors, there are some clear trends.

Substance abuse: The most robust evidence of all single factors linking schizophrenia and violence is substance abuse. However, substance abuse is more like a comorbid condition of the disease, and is therefore of limited interest in this assessment of independent psychological factors that represent an increased risk of violence.

Treatment: A substantial proportion of schizophrenia patients commit the act of violence before presenting for treatment. Nearly 40% of all homicides committed by people with schizophrenia take place during the first episode of the illness.

Childhood abuse: It appears that violence is only moderately associated with physical or sexual abuse.

Positive symptoms: A high percentage of patients who have committed serious violent acts report auditory hallucinations and/or delusional beliefs. However, the quantitative analysis (Figure 2) indicates that the association between severe violence and auditory hallucination/delusional beliefs is of moderate strength. The two symptoms are closely linked in schizophrenia. Auditory hallucinations often give rise to persecutory delusional beliefs.

Insight: Poor insight has been found to be associated with violence in many studies, but not consistently in all studies. A well-conducted meta-analysis (2) shows a strong effect size for insight. Lack of insight seems to have a more significant effect on violence than the positive symptoms.

Impulsivity: There have been some conflicting results regarding this clinical trait. Even so, we must note that a comprehensive meta-analysis (2) in which 11 studies were included, concluded that there is a strong association between poor impulse control and risk of violence in individuals diagnosed with psychosis; likewise, a highly significant OR was found

in the Verma et al. (2005) study, which had an adequate design and adequate number of patients. Also, the two studies together provide a strong support for poor impulse control as a significant risk factor.

Psychopathy: Nearly all studies have found a strong association between violence and psychopathy, although there is an exception (18). A serious limitation of this study is, however, that psychopathy was not assessed by a valid instrument.

Cognition: This is a complex construct, and the results are inconsistent. The strongest evidence for an association with violence has been found for motor speed and global cognition. This conclusion is primarily based on two recent studies with relevant designs (42, 44). To what extent poor executive function is a risk factor, is currently uncertain. It might be that impairments in executive functioning predispose patients to aggression by contributing to hostile attribution biases through a misinterpretation of real cues and an inability to update and modify cognition accordingly (49, 50). Social cognition has proved to be a promising risk factor, but has only been investigated in a small number of studies.

Limitations and strengths: One limitation is that a meta-analysis is lacking. Another is that in some of the studies, it is not specified whether one has studied violence in general or severe violence. Finally, the review has been confined to the past 20 years. The strength of the present review is that more psychological factors have been combined and compared in one review than in any other review before in this area.

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Figure Legends

Figure 1: PRISMA flow diagram of the systematic review

Figure 2 a,b: Forest plot of risk of severe violence in schizophrenia as odds ratio (ORs) according to 8 clinical and cognitive domains