# Risk and neurobiology of violence in schizophrenia:

*Multidisciplinary perspectives for forensic psychiatrists and law enforcement officials*

**Noel Shafi, M.S., University at Buffalo, College of Arts and Sciences**

May 2018

University at Buffalo
The State University of New York

## Introduction

### SCHIZOPHRENIA

Schizophrenia (SCZ) is a mental disorder characterized by positive symptoms such as delusions or hallucinations, disorganized symptoms such as disorganized thinking and abnormal motor behavior, and negative symptoms, such as social withdrawal, flat affect, or anhedonia. The prevalence rate of SCZ is about 4-7 per 1,000 persons (Saha, 2005).

### VIOLENCE

An operational definition of violent behavior is warranted in order to help to clarify the term. Violence in patients with SCZ can be defined as "hostile conducts on symptomatic stages of the disease like psychomotor agitation, verbal violence [and] aggressive behaviors" (Darmedru et al., 2017). These acts of aggression can range anywhere from verbal threats to physical aggression with fatal outcomes.

### SCHIZOPHRENIA AND VIOLENCE

Psychiatric research has demonstrated an increased risk of violence, particularly homicidal violence, in patients with psychotic disorders. This fact should not be used to generalize violence behaviors to all patients with mental illness. It is important to recognize the stigma of mental illness, and attributing violence to patients based on their mental health background is unwarranted. The vast majority of patients with mental illnesses are nonviolent. However, there is an increased probability of violence in patients with SCZ, which raises some concerns. Unraveling some of the risk factors of violence in SCZ can help mental health professionals, clinical researchers, law enforcement agencies, community health organizations, and social policy-makers to take appropriate measures that would help prevent violence or effectively treat patients with a history of or propensity for violence. It should be remembered, however, that patients with SCZ are more likely to be victims of violence than perpetrators of violence (Cutler, 2014).

### SCHIZOPHRENIA AND LAW ENFORCEMENT

Understanding violence in SCZ is also important for both forensic psychiatrists and law enforcement personnel in order to provide the best possible services to these patients from both a clinical and rehabilitative perspective. About 1% of all encounters between police and the general public involve a person with mental illness, and nearly 25% of all patients with mental illness have a history of police arrest (Livingston, 2016). In a minority of cases where patients with SCZ are prone to violence, police officers may exercise certain strategies to manage their behavior before it escalates, highlighting the importance of Crisis Intervention Team training (Demir et al., 2009; Compton et al., 2011). Previous research has found that patients with SCZ experiencing a psychotic episode for the first time are more likely to come into contact with police than the non-mentally ill, more than half of these encounters between police and SCZ involved patients with untreated psychosis, and that patients with SCZ were more likely to exhibit positive symptoms, such as delusions and hallucinations (Schumann et al., 2017).

### VIOLENCE IN THE UNITED STATES

The overall violent crime rate in the United States in 2016 was 386.3 per 100,000 inhabitants in 2016. Violent crime includes murder, manslaughter, rape, robbery, and aggravated assault. In particular, the murder rate in the U.S. in 2016 was 5.3 per 100,000 inhabitants in 2016 (FBI, 2017).

## Methods

### PURPOSE

This study aims to understand the neurobiology and risk of violence in SCZ and to use current findings to help inform the best practice for mental health professionals and law enforcement officials.

### DESIGN

This study is a selected literature review of major review articles in the psychiatric literature concerning violence in patients with SCZ.

### DATABASE

A computerized search was performed in PubMed.

### INCLUSION CRITERIA

Full-text, scholarly review articles published in English within the last 15 years, from 2003 to April 2018.

### KEYWORDS

The computerized keyword search on PubMed was divided into two phases:

Phase I: The search terms "violence" or "violent" combined with "schizophrenia" were entered in the title fields. All results were screened via full-text, if available. Some articles were excluded from this study due to unavailability or irrelevance to the research topic.

Phase II: The search terms "violence" or "violent" combined with "schizophrenia" and "police" were entered in the title fields. All results were screened via full-text, if available.

## Risk Factors

Numerous risk factors have been identified in association with violence and patients with SCZ, including treatment history, genetics, symptomatology, personality, cognition, neurobiology, demographics, history of violence, and substance abuse.

### TREATMENT HISTORY

Untreated SCZ patients are more likely to result in violence than their treated counterparts (Bo et al., 2011). In fact, most patients with SCZ who commit violence, specifically, a criminal offense, do so prior to their first contact with a mental health professional (Hodgins et al., 2017). Nonadherence to treatment is also associated with increased violence in SCZ (Topiwala et al., 2011).

### GENETICS

The catechol-O-methyl transferase (COMT) gene is one of several candidate genes associated with violence in SCZ. However, there have been conflicting reports on the role of COMT in SCZ (Hodgins et al., 2017). Still, the COMT genotype is believed to be "the best biological hypothesis for explaining aggressive behavior in SCZ" (Soyka et al., 2011). COMT is an enzyme responsible for metabolizing dopamine. Any abnormality in COMT structure may impair its function, resulting in abnormally increased dopamine levels, which is a common feature of SCZ neuropathology.

MAO-A is also believed to contribute to violence and aggression in SCZ. MAO-A is an enzyme involved metabolizing several neurotransmitters, including dopamine and serotonin (Soyka et al., 2011), both of which have been widely implicated in SCZ neuropathology. The same authors reviewed articles which found increased plasma levels of neuroactive steroids, such as allopregnanolone, in patients with SCZ who exhibited a higher rate of aggressiveness. Interestingly, allopregnanolone is known to modulate the GABA-a receptor, and GABA-ergic neurotransmission is a key element in the neurobiology of aggression.

### SYMPTOMALOGY

Positive symptoms of SCZ are associated with violent behavior. Some positive symptoms that are predictive of future violence include persecutory ideations, command hallucinations, and threat/control override symptoms. Negative symptoms, such as social withdrawal and flat affect are negatively correlated with violent behavior in SCZ.

### PERSONALITY DISORDERS

Patients with SCZ who have a comorbid personality disorder, particularly, psychopathic personality disorder, or who present with psychopathic traits, or with early onset anti-social behavior, also have a heightened risk for violence. Personality pathology in patients with SCZ is believed to be a stronger risk factor for violence than psychotic symptoms (Bo et al., 2011). Violence in SCZ may be associated with premorbid antisocial conduct (Volavka et al., 2013).

### SOCIAL COGNITION

Patients with SCZ have difficulty with perceiving other people's intentions and facial expressions or may overreact to negative affective expressions. There is conflicting evidence as to whether impaired empathy in SCZ mediates violent behavior in SCZ (Bragado, 2012; Darmedru et al., 2017).

### NEUROCOGNITION

Lack of insight, global cognitive impairment, executive impairments, working memory impairments, impulsivity, and cognitive inflexibility were also identified as risk factors for violence in SCZ (Darmedru et al., 2017).

### NEUROBIOLOGY

The neurobiology of violence and aggression is complex due to the heterogeneous nature of aggressive behaviors in humans. Several brain regions have been implicated in violence and aggression, including the amygdala, hippocampus, cingulate gyrus, thalamus, hypothalamus, and orbitofrontal cortex (Weiss, 2012). The aforementioned structures, with the exception of the orbitofrontal cortex, are part of the limbic system, which has been linked to emotion, memory, learning, arousal, and motivation. Similarly, another review found that reduced volume in the orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), and amygdala is associated with increased levels of aggression in clinical and nonclinical populations (Rosell and Siever, 2015). The reviewers note that the OFC and ACC are involved in sensory and cognitive processes, respectively, while the amygdala is involved in emotional learning and memory. However, these structures are not necessarily linked to violence and aggression in SCZ. Neuroimaging research has limited data on the neural correlates of violence in SCZ.

In general, the frontotemporal circuitry, which is associated with executive functioning and emotional processing, appears to be significantly impaired in patients with SCZ and a history of violence and aggression. The hippocampus, associated with memory, appears to have reduced volume in patients with SCZ and a history of homicidal violence, (Naudts et al., 2006).

Various neurotransmitters have been linked to aggression in general, including serotonin, gamma-aminobutyric acid, glutamate, dopamine, and noradrenaline (Cutler, 2014), in addition to hormones such as vasopressin, cortisol, and testosterone (Rosell and Siever, 2015).

**Neurobiology of violence in schizophrenia**

| Brain structure | Pathology | Function |
|---|---|---|
| Orbitofrontal circuitry | Structural abnormalities, white matter abnormalities, and impaired connectivity | Executive functioning and emotional processing |
| (Left) Hippocampus | Reduced volume | Memory |
| Lateral ventricles | Enlarged; with increased volume of cerebrospinal fluid | Production of cerebrospinal fluid; protects brain from trauma and supplies nutrients |
| Prefrontal cortex | Reduced cerebral blood flow | Decision-making, social behavior |

*Based on a review by Naudt et al. 2006*

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## Risk Factors (continued)

### DEMOGRAPHICS

**Age:** Patients with SCZ are more likely to engage in violence at an earlier age of onset than their non-schizophrenic peers.
**Gender:** Male patients with SCZ are more likely to engage in violence than their female counterparts.
**Economics:** Patients with SCZ who are from a low socio-economic background are more likely to engage in violence.
**Social:** Violence in SCZ is more likely in patients who live with others than in patients who live alone. Families of patients with SCZ are more likely to present with antisocial behavior (Hodgins et al., 2017), which contributes to increased stress in these patients. The patient's social network may also worsen his/her symptoms if the family environment is prone to violence or drug use (Cutler, 2014).

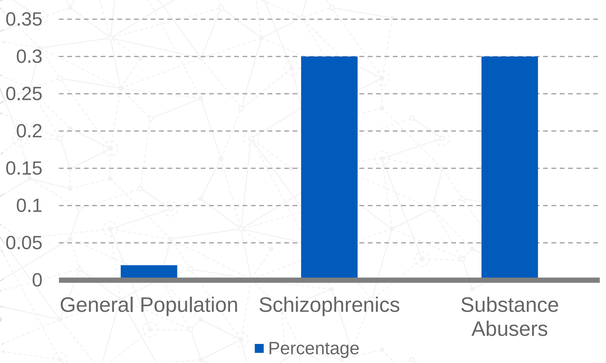
### HISTORY OF VIOLENCE

Patients with SCZ are more likely to engage in violence when they have a prior history of violence. Violent history may include early childhood trauma, prior exposure to violence, including domestic violence, previously committing acts of violence (Darmedru et al., 2017), and history of childhood physical or sexual abuse (Hodgins et al., 2017). A history of being convicted for threatening to kill is also associated with higher risk for patients with SCZ committing homicide in later years (Hodgins et al., 2017).

### SUBSTANCE ABUSE

Substance abuse accounts for a **majority** of the violence that occurs in patients with mental illnesses. Patients with SCZ and comorbid substance abuse are more likely to commit violence than patients with SCZ without comorbid substance abuse. Substance abuse comorbidity is one of the strongest predictors of violence in SCZ, but it is not the only risk factor, (Bo et al., 2011). Patients with a history of substance abuse have a similar rate of violence to patients with SCZ, but both groups have a substantially greater risk of violence overall than that of the general population (Fazel et al., 2009). Chronic alcohol and methamphetamine abuse often increase the risk of violence in patients (Cutler, 2014)

### RISK OF HOMICIDAL VIOLENCE




*Based on data from Fazel et al. (2009)*

## Conclusions

### PSYCHIATRIC RECOMMENDATIONS

Medical and psychosocial intervention for patients with SCZ and a history of violence should consider the aforementioned risk factors. Psychiatric treatment can address some risk factors but not others. There are two categories of risk factors, static risk factors and dynamic risk factors (Dermedru et al., 2017). Factors relating to genetics, gender, age, history of violence, and stable personality traits are static, and cannot be changed by psychotherapy or antipsychotic medication. Whereas factors relating to psychotic symptoms, cognition, biology, and some personality features are dynamic, and can be altered.

Recommendations for managing violence in SCZ include:

1. Psychotherapy
2. Antipsychotic Medication
3. Violence Risk Assessment

Evidence-based psychotherapy includes cognitive remediation and social cognitive skills training for patients with SCZ (Darmedru et al., 2017). Evidence-based antipsychotic medication includes clozapine, which is the most highly recommended and efficacious drug in reducing violent behaviors and stabilizing other related symptoms in patients with SCZ (Topiwala et al., 2011). Valproate or carbamazepine may also be added to the antipsychotic regimen to reduce impulsive aggression in some patients with SCZ (Volavka and Citrome, 2008).

Assessment for violence risk in patients with SCZ should also be considered, although direct evidence supporting the utility of current assessment tools for violence risk is lacking (Singh, 2011). Clinical researchers should consider the development of violence risk assessment tools specific to SCZ or examine currently available tools for their psychometric properties and predictive accuracy.

### LAW ENFORCEMENT RECOMMENDATIONS

Recommendations for managing violence in SCZ include:

1. Continue to use Crisis Intervention Team training or any other evidence-based mental health training program.
2. Refer patients to psychiatric facilities as deemed appropriate by the officer and mental health partner.
3. Minimize arrests and use of force if possible, without jeopardizing the safety of the officer, patient, or others.
4. Collaborate with mental health providers and the local community for implementing policies that would help rehabilitate the patient with mental illness.
5. Continue to implement community policing programs with a focus on prevention and treatment of drug use.
6. Create a taskforce to stop the flow of methamphetamine, a stimulant drug associated with increased violence.

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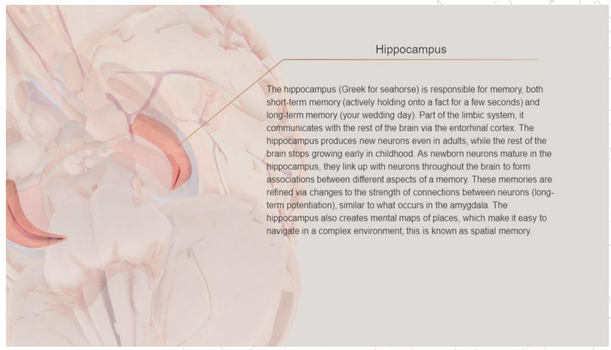
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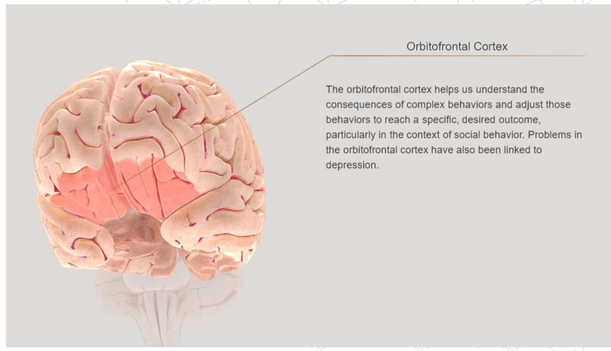
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## Brain Models




*Hippocampus. © Society for Neuroscience (2017)*




*Orbitofrontal Cortex. © Society for Neuroscience (2017)*

## Contact

noelshafi@buffalo.edu