Published in final edited form as:

Schizophr Res. 2018 May ; 195: 136–141. doi:10.1016/j.schres.2017.10.002.

Predictors of aggression in 3.322 patients with affective disorders and schizophrenia spectrum disorders evaluated in an emergency department setting

Emily Blanco, BA^a, Laura M. Duque, MD^b, Vivekananda Rachamallu, MBBS^c, Eunice Yuen, MD, PhD^d, John Kane, MD^{e,f,g}, and Juan A. Gallego, MD, MS^{e,f,g}

^aWeill Cornell Medical College, New York, NY, USA

^bUniversidad CES, Medellín, Antioquia, Colombia

^cTexas Tech University, Lubbock, TX, USA

^dYale University, New Haven, CT, USA

^eHofstra Northwell School of Medicine, Hempstead, NY, USA

^fThe Feinstein Institute for Medical Research, Manhasset, NY, USA

^gThe Zucker Hillside Hospital, Glen Oaks, NY, USA

Abstract

Introduction—The aim of this study is to determine odds of aggression and associated factors in patients with schizophrenia-spectrum disorders (SSD) and affective disorders who were evaluated in an emergency department setting.

Methods—A retrospective study was conducted using de-identified data from electronic medical records from 3.322 patients who were evaluated at emergency psychiatric settings. Data extracted included demographic information, variables related to aggression toward people or property in the past 6 months, and other factors that could potentially impact the risk of aggression, such as comorbid diagnoses, physical abuse and sexual abuse. Bivariate analyses and multivariate regression analyses were conducted to determine the variables significantly associated with aggression.

Address correspondence and reprint requests to: **Juan A. Gallego**, New York-Presbyterian Hospital Westchester Division, 21 Bloomingdale Rd., White Plains NY 10605, jug9069@med.cornell.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Contributors

Author Emily A. Blanco conducted statistical analysis and wrote the first draft of the manuscript. Authors Laura Duque, Vivek Rachamallu, and Eunice Yuen set up and cleaned the database, conducted initial analyses and created the tables. Author John M. Kane provided guidance in designing the study and revised the manuscript. Author Juan A. Gallego designed the study wrote the protocol and revised the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of Interest

Emily Blanco, Laura Duque, Eunice Yuen, Vivek Rachamallu and Juan A. Gallego have no conflict of interest to disclose.

Results—An initial multivariate regression analysis showed that SSD had 3.1 times the odds of aggression, while bipolar disorder had 2.2 times the odds of aggression compared to unipolar depression. A second regression analysis including bipolar subtypes showed, using unipolar depression as the reference group, that bipolar disorder with a recent mixed episode had an odds ratio (OR) of 4.3, schizophrenia had an OR of 2.6 and bipolar disorder with a recent manic episode had an OR of 2.2. Generalized anxiety disorder was associated with lower odds in both regression analyses.

Conclusion—As a whole, the SSD group had higher odds of aggression than the bipolar disorder group. However, after subdividing the groups, schizophrenia had higher odds of aggression than bipolar disorder with a recent manic episode and lower odds of aggression than bipolar disorder with a recent mixed episode.

Keywords

aggression; unipolar depression; schizophrenia; bipolar disorder; emergency department

1. Introduction

Over the last decade, media reports of violence in the U.S. have focused in large part on mass shootings reportedly caused by individuals with mental illness, including the Aurora theater shooting, the Sandy Hook elementary school shooting and the Charleston church shooting to name a few. Such cases of gun violence have aired widely on cable news networks, with the consequence of broadly linking violent behavior with mental illness in public consciousness. Though most research finds an association between mental illness and violence, the precise nature of the relationship and the specificity of violence as a feature of certain psychiatric diagnoses remains unclear (Steadman, 1998; Mullen et al., 2000; Ballester et al., 2012). Efforts to elucidate the relationship between mental illness and violence include the seminal MacArthur Violence Risk Assessment study and its observation of the prevalence of community violence among those with a psychiatric diagnosis in a large sample of individuals discharged from an inpatient setting (Steadman et al., 1998). Data from the study showed that 28.5% of those diagnosed with unipolar depression committed an act of aggression in the year following discharge, compared to 22% of those diagnosed with bipolar disorder and 14.8% of those diagnosed with schizophrenia. However, researchers have since found differing rates and conditions of aggression among individuals with a psychiatric diagnosis and some even argue that mental illness is not indelibly associated with aggression (Mullen et al., 2000; Elbogen and Johnson, 2009; Nielssen et al., 2012). Despite that considerable heterogeneity exists amongst those diagnosed with schizophrenia and affective disorders, the ascertainment of accurate rates and conditions of aggressive behavior among those with such diagnoses can better inform risk assessment and public attitudes. We conducted an electronic medical records chart review to compare the odds of aggression between patients with schizophrenia spectrum disorders (SSD) and affective disorders who were evaluated in the emergency room of a tertiary hospital in New York. We hypothesized that those with a SSD would have a greater association with aggression compared to those with affective disorders.

2. Methods

A retrospective study was conducted using de-identified data from electronic health records (EHR) from patients evaluated at the Medical Emergency department at the Long Island Jewish Medical Center or the Health Evaluation Clinic (HEC) at The Zucker Hillside Hospital between August 3rd 2011 and July 5th 2012. The HEC is an evaluation center taking patients who “walk in” looking for psychiatric treatment as well as those brought in for evaluation by police and/or emergency medical services.

We obtained EHR from patients with ICD9 codes: 295.00–295.95 (schizophrenia spectrum disorders) or ICD9 codes: 296.00–296.99 and 311 (affective disorders). The data extracted were obtained from the initial comprehensive psychiatric evaluation, which was conducted by an attending psychiatrist or a psychiatry resident supervised by an on-site psychiatrist. Data included (1) demographic information, (2) co-morbid diagnoses (3) current and recent homicidal thoughts and aggressive behavior; (4) current stressors at the time of the evaluation and (5) other factors including a history of abuse or neglect. Self-report was the primary means of collecting data. Of note, only a subset of patients responded to questions related to physical abuse, sexual abuse or neglect. No post-hoc definitions of homicidal ideation, intent, or plan or aggression were used for the analyses. Data regarding suicidal ideation and behavior was also collected and has been previously published (Gallego et al., 2015). We obtained information regarding patient diagnosis directly from the EHR. Of note, the psychiatric diagnosis was entered by clinicians in the EHR after performing the routine comprehensive psychiatric assessment. Given that our study used only de-identified data, it was deemed exempt from requiring IRB approval.

2.1 Analysis by diagnostic groups

Baseline characteristics were compared by diagnostic groups. To make this comparison we initially grouped the various diagnoses in the following manner.

The SSD group was comprised of the following diagnoses: 1) schizophrenia; 2) schizoaffective disorder; 3) schizophreniform disorder; 4) patients with a concomitant diagnosis of schizophrenia and bipolar disorder (given that some subjects had both diagnoses in the database at the same time) were considered to have schizoaffective disorder.

The primary affective disorder group included the following diagnosis: 1) bipolar disorder - most recent episode manic; 2) bipolar disorder - most recent episode depressed; 3) bipolar disorder - most recent episode mixed; 4) bipolar disorder not otherwise specified (NOS); 5) major depressive disorder; 6) depressive disorder NOS; 7) dysthymic disorder; 8) mood disorder NOS; 9) any combination of mood disorder diagnoses.

2.2 Analysis by aggression groups

Baseline characteristics were compared in two groups: 1) those with current or recent history of aggression (defined as aggressive behavior or thoughts within the last 6 months) and 2) those without either. Of note, the initial comprehensive psychiatric assessment conducted at the ED and HEC classified aggressive behavior as follows: 1) present; 2) unable to assess; 3) absent. Clinicians then had to choose between one of them at the time of the evaluation. For

purposes of our statistical analysis and in order to be conservative, we considered those in the “unable to assess” group as “absent”.

2.3 Statistical Analysis

Bivariate analyses were conducted examining the association between the two broad diagnostic groups (SSD vs. affective disorders) (Table 1) and aggression (Table 2) with other variables in the database. Categorical variables were compared using chi square test and continuous variables were compared using t-test for normality distributed variables or Wilcoxon rank-sum test for non-normally distributed variables.

A multivariate regression analysis was conducted to determine the variables that were independently associated with aggression. As a first step, we compared odds of aggression between SSD, bipolar disorder and unipolar depression using the latter as a reference group. We subsequently subdivided the SSD and bipolar disorder groups to study, in a second regression model, the potential differences between schizoaffective and bipolar disorder subtypes. The SSD group was subdivided into schizophrenia, schizoaffective disorder, bipolar type and schizoaffective disorder, depressed type. The bipolar disorder group was subdivided into bipolar disorder - most recent episode manic, bipolar disorder - most recent episode depressed and bipolar disorder - most recent episode mixed. To build the model, all variables statistically significant at a $p < 0.1$ level were included, as well as other variables, like age and sex, that could be related to the outcome. A logistic regression analysis using a manual backwards elimination approach was conducted. P values < 0.05 were considered significant (Table 3).

3. Results

3.1 Baseline Characteristics

Our sample comprised of 3,322 subjects, of which 46.7% were male and had a mean age of 35.2 years (SD=19.1). Five hundred and twenty-five individuals (15.8%) were considered to have current homicidal thoughts or aggressive behavior. Four hundred and fourteen (12.5%) patients had been aggressive to others in the past six months and 227 subjects (6.8%) had been aggressive towards property. In the six months prior to evaluation, 109 patients (3.3%) had only aggressive thoughts to others, while 305 (9.2%) had aggressive behavior towards others.

The following stressors were reported by patients at the time of the evaluation: financial or relationship losses (n=478, 14.4%), despair (n=234, 7.0%), health issues (n=223, 6.7%), anniversary of stress or loss (n=47, 1.4%) and recent humiliation and shame (n=188, 5.7%).

3.2 Baseline characteristics based on diagnostic groups

Two thousand four-hundred and two (2,402) subjects were classified as having a primary affective disorder and 920 were classified as having a SSD. The affective disorders group had a greater proportion of females (58.5%), while the SSD group was predominantly male (60.2%; $p < 0.001$). Patients in the SSD group were older (mean age: 41.5 years old, SD=15.0) compared to the other group (mean=32.9 years old, SD=19.2; $p < 0.001$). In the

SSD group, 39% of patients had schizophrenia (n=359), 60.5% had schizoaffective disorder (n=557) and 0.4% had schizophreniform disorder (n=4). Subjects with affective disorders had higher co-morbidity diagnosis rates: panic disorder (n=70/2402, 2.9%, $p<0.001$) post-traumatic stress disorder (n= 129/2402, 5.4%; $p<0.001$) anxiety NOS (n= 138/2402, 5.8%; $p<0.001$) and general anxiety disorder (GAD) (n=77/2402, 3.2%; $p<0.001$). In terms of current aggressive behavior, the SSD group, compared to the affective disorders group, had significantly higher rates of current homicidal/aggressive behavior (n=226/920, 24.6% vs. n=226/2402, 12.5%; $p<0.001$) and recent aggression to others (n=179/920, 19.5% vs. n=235/2402, 9.8%; $p<0.001$) or property (n=76/920, 8.3% vs. n=151/2402, 6.3%; $p<0.001$). This difference was present not only in aggressive behavior (n=50, 5.4% in SSD vs. n=59, 2.5% in affective disorders group) but also in aggressive thoughts (n=129, 13.0% vs. n=176, 7.3%; $p<0.001$). As per current stressors, the primary affective disorder group, compared to the SSD group, had significantly higher rates of despair (n=208/2402, 8.7% vs. n=26/920, 2.8%; $p<0.001$), health issues (n=183/2402, 7.6% vs. n=40/920, 4.4%; $p<0.001$), financial or relationship losses (n=428/2402, 17.8% vs. n=50/920, 5.4%; $p<0.001$) and anniversary of stress or loss (n=40/2402, 1.7% vs. n=7/920, 0.8%; $p=0.048$) (Table 1).

3.3 Baseline characteristics based on aggression

Patients in the Aggression group were mostly male (61%) compared to the No Aggression group, in which females were more common (56%). There were no statistical differences in age between the groups. The Aggression group compared to the No Aggression group had higher rates of bipolar disorder (n=145/525, 27.6% vs. n=623/2797 22.3%; $p=0.008$), schizophrenia (n=84/525, 16% vs. n=275/2797, 9.8%) and schizoaffective disorder (n=140/525, 27% vs. n= 417/2797, 14%) and lower rates of unipolar depression (n=76/525, 14.5% vs. n= 1100/2797, 39.3%; $p<0.001$) and dysthymic disorder (n=2/525, 0.4% vs. n=45/2797 1.6%; $p=0.029$).

With regard to comorbid anxiety disorders, the No Aggression group had higher rates of obsessive compulsive disorder (n= 90/2797, 3.2% vs. 1.5%; $p=0.035$), GAD (n= 80/2797, 2.9% vs. n=2/525, 0.4%; $p=0.001$) and anxiety disorder NOS (n=134/2797, 4.8% vs. n=12/525, 2.3%; $p=0.010$). In terms of current stressors, patients in the No aggression disorders group had higher rates of financial or relationship losses (n=420/2797, 15% vs. n=58/525, 11.1%; $p=0.017$) (Table 2). There were not statistically significant differences in rates of abuse or neglect between the Aggression and No Aggression groups.

3.4 Multivariate Regression Analysis

Our first regression analysis showed, after adjusting for sex and age, that a SSD diagnosis was associated with 3.1 times the odds of aggression compared to a unipolar depression diagnosis (95% CI: [2.41, 3.87]; $p<0.001$) whereas bipolar disorder was associated with 2.2 times the odds of aggression compared to unipolar depression (95%CI: [1.74, 2.86]; $p<0.001$). Conversely, a diagnosis of GAD (OR=0.19, 95%CI: [0.05, 0.77]; $p=0.02$) was associated with lower odds (Table 3).

We then subdivided the SSD and bipolar disorder groups for an additional multivariate analysis in order to assess odds of aggression among more specific diagnostic groups. Prior

to entering the variables in the model, we found that a large majority of those with a schizoaffective disorder did not have a bipolar type or depressed type entered in the EHR (549/557). Therefore, to be conservative, we did not include all those subjects with a schizoaffective disorder from this second regression analysis. Further, we found that 370 of the 768 with a bipolar diagnosis had an unspecified affective episode upon admission. We also decided not to include this group in the multivariate analysis in the interest of observing odds of aggression only among those diagnosed with a manic episode, a depressed episode, or a mixed episode upon admission. In total, we utilized the following diagnostic groups for the second multivariate analysis; schizophrenia, bipolar disorder - most recent episode manic, bipolar disorder - most recent episode depressed, bipolar disorder - most recent episode mixed, and unipolar depression, with the latter being the reference group.

After controlling for sex and age, results showed that a diagnosis of bipolar disorder - most recent episode mixed was associated with 4.3 times the odds of aggression compared to unipolar depression (95%CI: [2.58, 7.20]; $p<0.001$). Similarly, a diagnosis of schizophrenia was associated with 2.6 times the odds of aggression compared to unipolar depression (95%CI: [1.90, 3.50]; $p<0.001$) and a diagnosis of bipolar disorder - most recent episode manic was associated with 2.2 times the odds of aggression compared to unipolar depression (95%CI: [1.44, 3.29]; $p<0.001$). Conversely, a diagnosis of GAD (OR=0.22, 95%CI: [0.05, 0.89]; $p=0.034$) was associated with lower odds for aggression (Table 4).

4. Discussion

We conducted an electronic medical records chart review to compare odds of aggression between those with an SSD and those with affective disorders. We hypothesized that those with an SSD would have a greater association with aggression compared to those with affective disorders. Our initial multivariate analysis confirms this hypothesis. However, further analysis showed that a diagnosis of bipolar disorder - most recent episode mixed had higher odds of aggression than a diagnosis of schizophrenia and schizophrenia had higher odds of aggression than a diagnosis of bipolar disorder - most recent episode manic. Of note, we found that a diagnosis of bipolar disorder - most recent episode depressed was not a statistically significant predictor of aggression and it was dropped from the second regression analysis. Therefore, our data show that odds of aggression differ by the observation of more specific diagnostic categories.

Our finding that schizophrenia and bipolar disorder are associated with aggression has been previously described by other authors (Látalová, 2009; Mullen et al., 2000; Pulay et al., 2007; Volavka, 2013; Wallace and Wallace, 1998). However, our data do not support findings by other authors who found that those with a SSD and bipolar disorder are not independently associated with aggression (Nielssen et al., 2012; Elbogen and Johnson, 2009). Although a review of court documents concluded that the manic phase of bipolar disorder is not strongly associated with severe violence, the investigators studied a small sample ($n=272$) and restricted their definition of violence to include only homicide or attempted homicide causing serious physical injury (Nielssen et al., 2012). Further, Elbogen and Johnson (2009) did not find elevated risk for aggression in SSD or bipolar disorder patients compared to healthy controls. Instead, they conclude that aggression was associated with historical,

clinical, dispositional, and contextual factors including a history of violence, comorbid substance abuse, male sex, younger age, and recent divorce. However, individuals with a SSD or bipolar disorder may have an increased vulnerability to these contexts or stressors compared to the general population, making the study of both context and diagnosis relevant factors in the study of aggression.

Our data partially support findings by other authors stating that schizophrenia is associated with lower rates of aggression compared to individuals with a unipolar depression or bipolar disorder diagnosis (Steadman et al., 1998; Volavka, 2013). In our study, schizophrenia was associated with lower odds of aggression compared to bipolar disorder – most recent episode mixed. The reason behind this finding is unclear but we can speculate that it may related to an interaction between mania and depression. Typically, patients with depression alone tend to internalize anger but patients with co-occurring manic symptoms may be more prone to externalize anger and irritability.

Some studies have found that mixed episodes of bipolar disorder are associated with aggression (Binder et al., 1988; Cassidy et al., 1998; Látalová, 2009). However, to our knowledge, there is no available research directly comparing rates of aggression between mixed episodes of bipolar disorder and schizophrenia. Interestingly, we found that schizophrenia was associated with higher odds of aggression compared to mania. This is in contrast to the findings by Volavka (2013) who reviewed the literature and concluded that rates of violence were higher in bipolar disorder compared to schizophrenia, particularly during the manic phase. Given that the emergency department clinicians did not employ formal criteria to diagnose patients but rather used clinical judgment, it is possible that individuals who presented to the emergency department with irritability and dysphoria in the context of mania were more likely diagnosed by physicians as having bipolar disorder with a current mixed episode rather than a manic episode. Therefore, it is possible that odds of aggression among those classified as having bipolar disorder with a current manic episode could be attenuated in our study.

Our finding that a diagnosis of GAD is associated with lower odds of aggression is interesting given uncertainty about the association between GAD and aggression (Bubier & Drabick, 2009). GAD very often co-occurs with disorders like depression, other anxiety disorders and attention-deficit/hyperactivity disorder so the study of aggression in GAD in the absence of co-morbid diagnoses is necessary. However, our finding supports a claim that individuals sensitive to anxiety may avoid the unpleasant anxiety-related physiological sensations that characterize aggression (Broman-Fulks et al., 2007).

A strength of our study includes the description of a large and representative sample of 3,322 patients with a diagnosis of a SSD or an affective disorder from a metropolitan area. We did not find any other comparable studies observing odds of aggression in a sample of individuals evaluated at an emergency department beyond those focused on studying aggression within the emergency department setting. Much of the research done on the association between mental illness and aggression has taken place in either inpatient hospital settings or in the criminal justice system, which could result in biased estimates of aggression (Elliot et al., 1986; Robins & Reiger, 1991; Harris and Rice, 1997; Nielssen et

al., 2012). Further, “aggression” is defined in this study as both thoughts and behavior, broadly encompassing both the potential for and the actualization of aggressive behavior. This is in contrast to other studies that used a very restrictive definition of aggression, such as an indicted offense.

Our study has some limitations. Self-report was exclusively used to gather data about aggression, with the potential effect of patients inaccurately reporting their aggression. Second, our data was retrospectively collected, so information about diagnosis was not fully documented, as evidenced by the lack of documentation about the subtypes of bipolar disorder and schizoaffective disorder. Information regarding substance abuse was not systematically collected in our study and therefore we cannot assess its impact on our findings. This is unfortunate, given that substance abuse has been found to significantly raise the likelihood of aggression in people with and without a psychiatric diagnosis (Elbogen and Johnson, 2009; Ballester et al., 2012; Mullen et al., 2000, Steadman et al., 1998). For the same reason, we lack data related to co-morbid personality disorders, though these conditions have been linked to increased rates of aggression as well (Gilbert et al., 2015; Volavka, 2013).

As aggression is a complex human behavior, the sole use of clinical information may not be sufficient to explain it. Neuroimaging (Soyka, 2011; Hoptman & Antonius, 2015), genetic (Hong et al. 2008; Chung et al., 2010), and molecular (Nelson & Chiavegatto, 2001) studies have been conducted to try to elucidate the biology of aggression generally and in those with psychiatric diagnoses, though questions still remain. A broad integration of these techniques can help us to understand how aggression is precipitated and if individuals with psychiatric disorders confer a unique biological risk for aggressive behavior compared to the general population.

Acknowledgments

None

Funding body agreements and policies

This study was supported in parts by the National Institute of Mental Health (K23MH100264 to J.A.G).

Dr. Kane has been a consultant for or received honoraria from Alkermes, Eli Lilly, EnVivo Pharmaceuticals (Forum), Forest (Allergan), Genentech, H. Lundbeck, Intracellular Therapies, Janssen Pharmaceutica, Johnson and Johnson, Neurocrine, Otsuka, Pierre Fabre, Reviva, Roche, Sunovion, Takeda and Teva. He has received grant support from Otsuka and Janssen and has participated in Advisory Boards for Alkermes, Intracellular Therapies, Lundbeck, Neurocrine, Otsuka, Pierre Fabre, Takeda, and Teva. He is a shareholder in MedAvante, Inc., Vanguard Research Group and LB Pharmaceuticals, Inc.

References

- Ballester J, Goldstein T, Goldstein B, Obreja M, Axelson D, Monk K, Hickey M, Iyengar S, Farchione T, Kupfer DJ, Brent D, Birmaher B. 2012; Is bipolar disorder specifically associated with aggression? *Bipolar Disorders*. 14(3):283–290. [PubMed: 22548901]
- Binder RL, McNiel DE. 1988; Effects of diagnosis and context on dangerousness. *American Journal of Psychiatry*. 145:728–32. [PubMed: 3369561]
- Broman-Fulks J, McCloskey M, Berman M. 2007; Anxiety sensitivity and retaliatory aggressive behavior in research volunteers. *Aggressive Behavior*. 33(2):137–144. [PubMed: 17441014]

- Bubier JL, Drabick DAG. 2009; Co-occurring Anxiety and Disruptive Behavior Disorders: The Roles of Anxious Symptoms, Reactive Aggression, and Shared Risk Processes. *Clinical Psychology Review*. 29(7):658–669. [PubMed: 19729235]
- Cassidy F, Murry E, Forest K, Carroll BJ. 1998; Signs and symptoms of mania in pure and mixed episodes. *Journal of Affective Disorders*. 50:187–201. [PubMed: 9858078]
- Chung S, Chung HY, Jung J, Chang JK, Hong JP. 2010; Association among aggressiveness, neurocognitive function, and the Val66Met polymorphism of brain-derived neurotrophic factor gene in male schizophrenic patients. *Comprehensive Psychology*. 51(4):367–72.
- Elbogen C, Johnson S. 2009; The intricate link between violence and mental disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Archives of General Psychiatry*. 66(2):152–61. [PubMed: 19188537]
- Elliott D, Huizinga D, Morse B. 1986; Self-reported violent offending: a description analysis of juvenile violent offenders and their offending careers. *Journal of Interpersonal Violence*. 1:472–513.
- Gallego JA, Rachamalla V, Yuen EY, Fink S, Duque LM, Kane JM. 2015; Predictors of suicide attempts in 3,322 patients with affective disorders and schizophrenia spectrum disorders. *Psychiatry Research*. 228(3):791–796. [PubMed: 26077849]
- Gilbert F, Daffern M, Talevski D, Ogloff JR. 2015; Understanding the personality disorder and aggression relationship: an investigation using contemporary aggression theory. *Journal of Personality Disorders*. 29(1):100–14. [PubMed: 23398093]
- Harris GT, Rice ME. 1997; Risk appraisal and management of violence behavior. *Psychiatry Services*. 48(9):1168–117.
- Hong JP, Lee JS, Chung S, Jung J, Yoo HK, Chang SM, Kim CY. 2008; New functional single nucleotide polymorphism (Ala72Ser) in the COMT gene is associated with aggressive behavior in male schizophrenia. *American Journal of Medical Genetics*. (5):658–60.
- Hoptman M, Antonius D. 2015; Neuroimaging correlates of aggression in schizophrenia: an update. *Current Opinions in Psychiatry*. 24(2):100–106.
- Látalová K. 2009; Bipolar disorder and aggression. *International Journal of Clinical Practice*. 63:889–899. [PubMed: 19490199]
- Mullen P, Burgess P, Wallace C, Palmer S, Ruschena D. 2000; Community care and criminal offending in schizophrenia. *Lancet Psychiatry*. 355:614–617.
- Nelson R, Chiavegatto S. 2001; Molecular basis of aggression. *Trends in Neuroscience*. 24(12):713–719.
- Nielsen O, Malhi G, Large M. 2012; Mania, homicide, and severe violence. *Australian and New Zealand Journal of Psychiatry*. 46:357–363. [PubMed: 22508595]
- Pulay AJ, Dawson DA, Hasin DS. 2007; Violent behavior and DSM-IV psychiatric disorders: results from the national epidemiologic survey on alcohol and related conditions. *Journal of Clinical Psychology*. (12):e1–11.
- Robins, L, Reiger, D. *Psychiatric Disorders in America*. New York, NY: The Free Press; 1991.
- Soyka M. 2011; Neurobiology of aggression and violence in schizophrenia. *Schizophrenia Bulletin*. 37(5):913–920. [PubMed: 21860037]
- Steadman H, Mulvey E, Monahan J, Robbins P, Appelbaum P, Grisso T, Roth L, Silver E. 1998; Violence by people discharged from acute psychiatric inpatient facilities and by others in the same neighborhoods. *Archives of General Psychiatry*. 55:393–401. [PubMed: 9596041]
- Volavka J. 2013; Violence in schizophrenia and bipolar disorder. *Psychiatria Danubina*. 25(1):24–33. [PubMed: 23470603]
- Wallace D, Wallace R. 1998; Scales of Geography, Time, and Population: The study of violence as a public health problem. *American Journal of Public Health*. 88:1852–1858.

Table 1

Baseline characteristics on diagnostic based groups

Variable	All sample (N=3,322)	Affective disorders (N=2,402)	Schizophrenia spectrum disorders (N=920)	p-value
Sex, Male (%)	1,551 (46.7)	997 (41.5)	554 (60.2)	<0.001
Age, mean years (SD)	35.2(19.1)	32.9(19.9)	41.5(15.0)	<0.001
<i>Co-morbid Diagnoses</i>				
Unipolar depression, n(%)	1,176 (35.4)	1,176 (49.0)	0 (0.0)	
Bipolar, n(%)	768 (23.1)	768 (32.0)	0 (0.0)	
Manic	174 (5.27)	174 (7.29)	0 (0.0)	
Depressive	148 (4.46)	148 (6.16)	0 (0.0)	
Mixed	76 (2.32)	76 (3.21)	0 (0.0)	
Unspecified	370 (11.08)	370 (15.32)	0 (0.0)	
Depression NOS, n(%)	77 (2.3)	77 (3.2)	0 (0.0)	
Mood disorder NOS, n(%)	687 (20.7)	687 (28.6)	0 (0.0)	
Dysthymic disorder, n(%)	47 (1.4)	47 (2.0)	0 (0.0)	
SSD, n(%)	920 (27.7)	0 (0.0)	920	
Schizophrenia, n(%)	359(10.8)	0 (0.0)	359 (39.0)	
Schizoaffective, n(%)	557 (16.8)	0 (0.0)	557 (60.5)	
Schizophreniform Disorder, n(%)	4 (0.1)	0 (0.0)	4 (0.4)	
PTSD, n(%)	143 (4.3)	129 (5.4)	14 (1.5)	<0.001
Panic Disorder, n(%)	75 (2.3)	70 (2.9)	5 (0.5)	<0.001
OCD, n(%)	98 (3.0)	79 (3.3)	19 (2.1)	0.062
GAD, n(%)	82 (2.5)	77 (3.2)	5 (1.0)	<0.001
Anxiety NOS, n(%)	146 (4.4)	138 (5.8)	8 (1.0)	<0.001
<i>Aggression Variables</i>				
Current homicidal aggression/aggressive behavior, n(%)	525 (15.8)	299 (12.5)	226 (24.6)	<0.001
Aggression to others (past 6 months), n(%)	414 (12.5)	235 (9.8)	179 (19.5)	<0.001
Only thoughts, n(%)	109 (3.3)	59 (2.5)	50 (5.4)	<0.001
Behavior, (n)%	305 (9.2)	176 (7.3)	129 (13.0)	<0.001
Aggression to property (past 6 months), n(%)	227 (6.8)	151 (6.3)	76 (8.3)	0.044
Only thoughts, n(%)	12 (0.4)	9 (0.4)	3 (0.3)	0.205
Behavior, n(%)	161 (4.9)	107 (4.5)	54 (5.9)	0.205
<i>Current Stressors</i>				
Despair, n(%)	234 (7.0)	208 (8.7)	26 (2.8)	<0.001
Health Issue, n(%)	223 (6.7)	183 (7.6)	40 (4.4)	0.001
Losses (financial or relationships), n(%)	478 (14.4)	428 (17.8)	50 (5.4)	<0.001
Anniversary of stress or loss, n(%)	47 (1.4)	40 (1.7)	7 (0.8)	0.048
<i>Other factors</i>				
Physical abuse*, n(%)	215 (22.2) [967]	173 (23.1)	42 (19.4)	0.247
Sexual abuse*, n(%)	232 (24.2) [958]	190 (25.6)	42 (19.6)	0.069

Variable	All sample (N=3,322)	Affective disorders (N=2,402)	Schizophrenia spectrum disorders (N=920)	p-value
Neglect*, n(%)	41 (5.0) [814]	32 (5.1)	9 (4.8)	0.844

^aMDD: Major Depressive Disorder;

^bNOS: Not Otherwise Specified;

^cPTSD: Post-traumatic stress disorder;

^dOCD: Obsessive Compulsive Disorder;

^eGAD: Generalized Anxiety Disorder.

^f[]: Number of subjects for which data was entered.

^gVariables where data was not collected from all subjects.

Table 2

Baseline characteristics based on aggression groups

Variable	No aggression (N=2,797)	Aggression (N=525)	p value
Sex, Male (%)	1,231 (44.0)	320 (61.0)	<0.001
Age, median years (IQR)	32 (18–50)	29 (20–46)	0.4
Co-morbid Diagnoses			
Unipolar depression, n(%)	1,100 (39.3)	76 (14.5)	<0.001
Bipolar, n(%)	623 (22.3)	145 (27.6)	0.008
Manic	139 (4.9)	35 (6.6)	0.007
Depressed	133 (4.8)	15 (2.9)	0.350
Mixed	53 (1.9)	23 (4.4)	<0.001
Depression NOS, n(%)	69 (2.5)	8 (1.5)	0.188
Mood disorder NOS, n(%)	570 (20.4)	117 (22.3)	0.322
Dysthymic disorder, n(%)	45 (1.6)	2 (0.4)	0.029
Diagnosis:			
Schizophrenia, n(%)	275 (9.8)	84 (16)	<0.001
Schizoaffective, n(%)	417 (14)	140 (27)	
Schizophreniform Disorder, n(%)	3 (.01)	1 (.01)	
Mood disorders, n(%)	2102 (75.2)	300 (57.1)	
PTSD, n(%)	124 (4.4)	19 (3.6)	0.399
Panic Disorder, n(%)	68 (2.4)	7 (1.3)	0.120
OCD, n(%)	90 (3.2)	8 (1.5)	0.035
GAD, n(%)	80 (2.9)	2 (0.4)	0.001
Anxiety NOS, n(%)	134 (4.8)	12 (2.29)	<0.010
Aggression Variables			
Aggression to others (past 6 months), n(%)	0 (0.0)	414 (78.9)	NA
Only thoughts, n(%)	0 (0.0)	109 (20.8)	NA
Behavior, n(%)	0 (0.0)	305 (58.1)	NA
Aggression to property (past 6 months), n(%)	0 (0.0)	227 (43.2)	NA
Only thoughts, n(%)	0 (0.0)	12	NA
Behavior, n(%)	0 (0.0)	215	NA
Current Stressors			
Despair, n(%)	203 (7.3)	31 (6.0)	0.266
Health Issue, n(%)	196 (7.0)	27 (5.1)	0.117
Losses (financial or relationships), n(%)	420 (15.0)	58 (11.1)	0.017
Anniversary of stress or lost, n(%)	38 (1.4)	9 (1.7)	0.527
Other Factors			
Physical abuse*, n(%)	171 (21.5)	44 (25.4)	0.264
Sexual abuse*, n(%)	185 (23.5)	47 (27.5)	0.271
Neglect*, n(%)	30 (4.5)	11 (7.6)	0.116

^a MDD: Major Depressive Disorder;^b NOS: Not Otherwise Specified;

^cPTSD: Post-traumatic stress disorder;

^dOCD: Obsessive Compulsive Disorder;

^eGAD: Generalized Anxiety Disorder.

^f[]: Number of subjects for which data was entered.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 3

Multivariate Regression Analysis – Predictors of Aggression (n= 3,322)

	OR	95% CI	p-value
Sex	.5865279	.4819135, .713852	0.000*
Schizophrenia-spectrum Disorders	3.055957	2.414586, 3.867691	0.000*
Bipolar Disorder	2.230969	1.740374, 2.859857	0.000*
Generalized Anxiety Disorder	.1881295	.0457696, .7732808	0.021*
Age	.9893707	.9837315, .9950422	0.000*

^aUsing unipolar depression as a reference group;^bOR: Odds Ratio;^cCI: Confidence Interval

Table 4

Multivariate Regression Analysis – Predictors of Aggression (n=2,439)

	OR	95% CI	p-value
Sex	.5439584	.422654, .7000779	0.000*
Schizophrenia	2.576599	1.903241, 3.488189	0.000*
Bipolar Disorder (Manic)	2.176872	1.442192, 3.285811	0.000*
Bipolar Disorder (Mixed)	4.306463	2.575018, 7.202132	0.000*
Generalized Anxiety Disorder	.2156407	.052027, .8937843	0.034*
Age	.9924541	.985837, .9991156	0.026*

^aUsing unipolar depression as a reference group;^bOR: Odds Ratio;^cCI: Confidence Interval