

## ONLINE FIRST

## The Relationship Between Delusions and Violence

## Findings From the East London First Episode Psychosis Study

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**Importance:** Psychotic persons who are violent often explain their violence as being due to delusions. However, research has failed to confirm associations between delusions and violent behavior.

**Objectives:** To investigate which delusional beliefs and characteristics are associated with violent behavior during a first episode of psychosis and whether these associations are mediated by affect due to delusions.

**Design:** Population-based epidemiological survey of first-episode psychosis during a 2-year study period.

**Setting:** Three inner-city boroughs in East London, England.

**Participants:** A total of 458 patients with first-episode psychosis who were 18 to 64 years of age.

**Interventions:** Patients were clinically assessed (using the Schedules for Clinical Assessment in Neuropsychiatry and the Maudsley Assessment of Delusions Schedule) and interviewed about their displaying violent behavior while experiencing psychotic symptoms during the 12-month period prior to interview.

**Main Outcome Measures:** Violence was classified at 2 levels of severity: minor and serious violence.

**Results:** The prevalence of violence was 38% during the 12-month period, and 12% of the sample engaged in serious violence. Distinct sets of demographic and comorbid risk factors were associated with minor and serious violence. These were adjusted for in subsequent analyses. Anger was the only affect due to delusions that was positively associated with violence. The population-attributable risk percentage was 30.8% for minor violence and 55.9% for serious violence. A small number of uncommon delusional beliefs demonstrated direct pathways leading to minor violence. Three highly prevalent delusions demonstrated pathways to serious violence mediated by anger due to delusional beliefs: persecution ( $z=3.09, P=.002$ ), being spied on ( $z=3.03, P=.002$ ), and conspiracy ( $z=2.98, P=.002$ ).

**Conclusions and Relevance:** Anger due to delusions is a key factor that explains the relationship between violence and acute psychosis. A subset of delusional beliefs may be causally linked to violence, and certain uncommon beliefs demonstrated a direct association with minor violence. Highly prevalent delusional beliefs implying threat were associated with serious violence, but they were mediated by anger.

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**D**ELUSIONS ARE CONSIDERED by many clinicians to be important causative factors for violent behavior during acute states of psychosis and are frequently given as explanations for violence by patients. Although early studies supported the notion that violence can be driven by symptoms of psychosis, including delusions,<sup>1-4</sup> threat/control override,<sup>5-8</sup> and command hallucinations,<sup>9,10</sup> others have failed to confirm these associations.<sup>11-15</sup> Furthermore, epidemiological studies demonstrated that the key risk factors for violence among persons with psychosis are the same as those among the general popu-

lation after adjustment for comorbid psychopathology.<sup>16-20</sup> However, a recent meta-analysis<sup>21</sup> supported a relationship between violence and psychosis, although effect sizes varied considerably depending on moderators such as design, measurement of psychosis, and outcome. It was recommended that future research should focus on specific diagnostic groups and clusters of psychotic symptoms. Other factors associated with psychotic symptoms may also be relevant, including affect. Earlier studies demonstrated that persecutory delusions were marked by negative affect and propensity to act,<sup>22</sup> and that patients who acted violently were more likely to report that delusions made them an-

gry.<sup>23</sup> In a study<sup>11</sup> of patients with delusions who were discharged from the hospital, the association between violence and threat/control override was explained by trait anger and impulsiveness. Furthermore, among patients at high risk for community violence, hostility predicted serious violence, but no association was found with threat/control, anxiety, depression, or general psychological distress.<sup>24</sup> These studies suggest that the association between delusions and violence is mediated by intermediate variables (negative affect/anger) that are not always present, but when they occur, they have a significant effect on violent outcome.

To our knowledge, no previous study has investigated the causal pathways from delusions to violence with the aim of identifying mediator variables. However, several pathways are possible: acting violently on the basis of a delusional belief could be (1) directly due to the content of the belief itself (direct pathway), (2) driven by affective symptoms that are another component of the psychotic illness, (3) explained by underlying personality traits such as anger, or (4) explained by the content and characteristics of the delusions that result in negative affect.

To investigate the causal pathways of psychotic symptoms and violent behavior, 2 main methodological problems must be overcome, the first of which is the failure to ensure critical timing of co-occurrence of delusions and violent outcome. Risk is greatest when symptoms are active.<sup>2,25-29</sup> Epidemiological studies<sup>16-18,20</sup> using diagnoses or symptoms measured at various points over the lifetime of the individual and comparing them with self-report or criminal records over extended periods have inevitably observed risk factors similar to the general population. Social decline secondary to psychosis, substance misuse, and antisocial lifestyle convey the greatest risk because any factors specifically associated with acute symptomatic disturbance will have operated only briefly and are unlikely to be captured in these studies. Second, few studies have differentiated a range of potential violent outcomes in terms of seriousness. Some have included verbally abusive, threatening behavior and even self-harm to increase statistical power.<sup>30,31</sup>

There is accumulating evidence that the period of acute psychotic disturbance prior to first contact with psychiatric services is specifically associated with an increased risk of serious violence.<sup>32</sup> Contact with psychiatric services is often initiated because of violence during a first episode of psychosis.<sup>3,15</sup> The East London First Episode Psychosis Study was designed to determine (1) whether there is a direct association between delusions and violence when they occur in close temporal proximity; (2) whether associations are confounded/mediated by affective symptoms, trait anger, or affect due to delusional beliefs; and (3) which delusional beliefs have the strongest effect on outcome (seriousness of violence).

## METHODS

### STUDY DESIGN AND SAMPLE

The East London First Episode Psychosis Study is a large, population-based incidence study that was conducted for 2 years in 3 neighboring boroughs in London, England. The area is an

exclusively inner-city urban area characterized by high levels of socioeconomic deprivation and ethnic density. The primary aim was to measure violent and aggressive behavior occurring before first contact with mental health services. Ethical approval was obtained from the local research ethics committee in East London.

## PROCEDURES

The sampling procedure has previously been described in detail.<sup>33,34</sup> In brief, all those patients 18 to 64 years of age living in the study area who made contact with mental health services (including forensic services and prisons) because of a first episode of any probable psychotic disorder were identified during study periods of 24 months in each borough between December 1, 1996, and November 30, 2000. Initial inclusion criteria were based on the World Health Organization<sup>35</sup> and the *Ætiology and Ethnicity in Schizophrenia and Other Psychoses* study.<sup>36</sup> Methods used by Cooper et al<sup>37</sup> were used to minimize leakage and identify patients missed by screening.

Patients who passed the screen underwent a battery of assessments. The Schedules for Clinical Assessment in Neuropsychiatry<sup>38</sup> are a set of instruments used to assess adult major psychiatric disorders. Researchers were trained in the Schedules for Clinical Assessment in Neuropsychiatry interview by taking a course approved by the World Health Organization, and established prestudy reliability using independent ratings of videotaped interviews.

The Maudsley Assessment of Delusions Schedule<sup>39</sup> is a reliable and valid assessment of delusional experiences and their possible consequences. The interview starts with the patients' spontaneous accounts of delusions with simple prompting questions to minimize interviewer bias. Domains covered include conviction, belief maintenance, affect relating to delusions, actions, preoccupation, systematization, and insight.<sup>22</sup>

Alcohol use disorder over the past year was measured by asking about problems encountered because of alcohol use, craving, tolerance, withdrawal, and drinking to relieve withdrawal. The number of positive answers was added to indicate the severity of alcohol use disorder (range, 0-7). Each participant was asked about substance use over the past year: heroin/morphine, other opiates, amphetamine, cocaine, crack cocaine, hallucinogens/lysergic acid diethylamide, 3,4-methylenedioxymethamphetamine (ecstasy), barbiturates, cannabis, sedatives, solvents, and other substances.

Antisocial personality disorder (ASPD) was assessed using the Structured Clinical Interview for *DSM-IV* Axis II Personality Disorders.<sup>40</sup> Anger as a personality trait was measured using the Novaco Anger Scale (total score).<sup>41</sup>

A schedule developed to record sociodemographic data was administered that included education, occupation, ethnicity, and marital status. Social class was assessed using the Standard Occupational Classification 1991,<sup>42</sup> an ordinal classification system: (I) professional occupations; (II) managerial and technical occupations; (III) skilled occupations, nonmanual and manual; (IV) partly skilled occupations; and (V) unskilled occupations. Patients who declined to be interviewed or who were rated only using case notes were not included in our study.

The interviewers were clinically experienced Clinical Research Fellows (psychiatrists) blind to the study hypothesis. Anger was measured in the context of delusional beliefs and independent of violent behavior prior to the interview. Questions about violent incidents in the past 12 months were asked at the end of the interview and included questions about violent victimization and perpetration of violence.

We classified violent behavior against the person at 2 levels of severity using the MacArthur Community Violence Interview.<sup>43</sup> Only incidents that occurred in the 12 months prior to the interview were included. Using all sources of information available, raters were instructed to establish whether the patient experienced psychotic symptoms at the time of the incident. Violent incidents were excluded if the patient was not psychotic at the time or was psychotic but had responded to violence directed toward him or her. When there was more than 1 violent incident, the most serious was selected according to the 3 categories assigned: (1) no violent behavior, (2) occurrence of minor violence (simple assault without injury or weapon use), and (3) serious violence (assault resulting in injury or involving use of a lethal weapon, threat with a lethal weapon, or sexual assault). The categories were mutually exclusive.

### STATISTICAL ANALYSES

For descriptive purposes, absolute (numbers) and relative (%) frequencies were reported for dichotomous/polytomous categorical variables, and mean values (standard deviations) were reported for variables on interval/ratio level. Group differences were established using binary logistic regression (dichotomous outcomes) and multinomial regression analyses (polytomous outcomes) with odds ratios (ORs) as indicators of the magnitude of effect. For polytomous outcome variables, a reference category was assigned (no violence) against which the remaining categories were statistically tested.

To investigate associations between delusions and violent outcome and to investigate the role of affect in this relationship, analyses were performed in 3 steps. In step 1, the multinomial model was run unadjusted to test univariate main effects of delusions/affect related to delusional beliefs on outcome. In step 2, confounders were identified by comparing the 3 outcome groups with respect to demographic and other variables known to be risk factors for violent behavior; these variables were then included as covariates.

A mediator variable (M) explains how and why an independent variable (Y) affects outcome (X). Identification of such relationships is fundamental to the development of causal pathways. To investigate mediating effects of one variable on another temporal precedence (X preceding Y), correlations between X and Y, between X and M, and between M and X have to be established.<sup>44,45</sup> Our measure of affect related to delusions implies temporal precedence. Steps 1 and 2 provided information about associations between delusions and outcome and between affect related to delusional beliefs and violence. In a third step, the relationship between affect due to delusions and the delusions themselves was investigated. To demonstrate mediation, it must be shown that inclusion of the mediator variable either completely eliminates the predictor-outcome association or indicates at least some meaningful attenuation of the linkage. To statistically test whether a variable significantly mediated the association between predictor and outcome, we standardized regression coefficients as recommended by MacKinnon and Dwyer<sup>46</sup> and conducted a Sobel test,<sup>47</sup> which provides a test value (z score) and a level of significance. To avoid problems of collinearity, analyses were run separately.

Owing to the complexity of the statistical models following inclusion of numerous covariates and a possible increase of type II error, we decided against an  $\alpha$  adjustment. A level of  $P < .05$  for statistical significance was adopted throughout. All statistical analyses were performed using SPSS, version 18 (SPSS Inc), and STATA, version 11 (StataCorp).

### SAMPLE CHARACTERISTICS

Of the 484 study participants, 14 had demonstrated violent behavior unrelated to mental illness. These were excluded from subsequent analyses. For 12 participants, either no information was available on violent incidents or they could not be interviewed. The final study sample included 458 individuals: Over half were men (280 [61.1%]) with a mean (SD) age of 30.7 (10.1) years. The sample was ethnically diverse with 166 white patients (36.2%), 153 black patients (33.4%), 110 Asian patients (24.0%), and 29 patients of other ethnic origin (6.3%). Many (216 patients [47.2%]) were designated social classes IV and V, with 78 patients being designated social class III (17.0%) and only 32 being designated social classes I and II (7.0%). A quarter (116 [25.3%]) were unclassified owing to long-term unemployment or retirement. Most (342 [74.7%]) received a diagnosis of non-affective psychosis according to *DSM-IV* (schizophrenia: 158 [34.5%]; delusional disorder: 28 [6.1%]; brief psychotic disorder: 43 [9.4%]; schizoaffective disorder: 86 [18.8%]; and psychotic disorder not otherwise specified: 27 [5.9%]); the remaining 25.3% (116 patients) received a diagnosis of affective psychosis (major depression with psychotic features: 66 [14.4%]; manic episode with psychotic features: 46 [10.0%]; and mood disorder not otherwise specified with psychotic features: 4 [0.9%]).

Comorbid ASPD was present in 43 patients (9.4%), and 193 patients (42.1%) reported drug misuse in the past year. The mean (SD) score of alcohol abuse disorder was 0.59 (1.76).

The majority of patients (283 [61.8%]) did not demonstrate violent behavior in the year before the interview. Approximately a quarter of the patients (121 [26.4%]) engaged in minor violence, and 54 (11.8%) engaged in serious violence.

### VIOLENT AND NONVIOLENT GROUPS

Compared with the nonviolent reference group, significantly more of the minor violence group were black (50 violent patients [41.3%] vs 85 nonviolent patients [30.0%]; OR, 1.83 [95% CI, 1.10-3.06];  $P = .02$ ), younger (mean [SD] age, 29.4 [10.3] years for violent patients vs 32.1 [10.3] years for nonviolent patients; OR, 0.97 [95% CI, 0.95-0.99];  $P = .02$ ), had comorbid ASPD (17 violent patients [14.3%] vs 13 nonviolent patients [4.7%]; OR, 3.36 [95% CI, 1.58-7.14];  $P = .002$ ), and used drugs over the past year (67 violent patients [55.8%] vs 98 nonviolent patients [34.6%]; OR, 2.39 [95% CI, 1.54-3.69];  $P < .001$ ). Groups did not differ regarding sex, social class, unemployment, or alcohol use.

Among the serious violent subgroup, significantly more were men than women (42 men [77.8%] vs 12 women [22.2%]; OR, 2.65 [95% CI, 1.34-5.25];  $P = .005$ ), younger (mean [SD] age, 26.5 [7.5] years; OR, 0.93 [95% CI, 0.90-0.97];  $P < .001$ ), had comorbid ASPD (13 patients [24.5%]; OR, 6.54 [95% CI, 2.83-15.15];  $P < .001$ ), and used drugs (28 patients [51.9%]; OR, 2.03 [95% CI, 1.13-

3.66];  $P=.02$ ). Compared with the reference group no differences were found regarding ethnicity, social class, unemployment, or alcohol use.

### AFFECT RELATED TO DELUSIONS AND VIOLENT OUTCOME

In the eTable (jamapsych.com), we show the association between affect related to delusions (measured using the Maudsley Assessment of Delusions Schedule) and violent outcome. No associations were found with elation, fear, or anxiety after adjustments. Depressed affect demonstrated a significant inverse association with both minor and serious violence.

Anger due to delusions was associated with both minor and serious violence and remained significant following adjustments. Inclusion of symptoms of mania or trait anger did not attenuate these associations. To estimate the burden of risk for violence due to anger related to delusions, we calculated the population-attributable risk percentage as recommended by Horwath and colleagues.<sup>48</sup> The unadjusted population-attributable risk percentage for minor violence was 39.7%. Adjustment for sex, ethnicity, age, comorbid ASPD, drug use, mania total score, and trait anger resulted in a population-attributable risk percentage of 30.8%. The unadjusted population-attributable risk percentage for serious violence was 57.8% with a minor decrease in magnitude following adjustment (55.9%). In subsequent analyses, anger due to delusions was considered a potential mediator in the pathway between delusions and violent outcome.

### DELUSIONS AND ANGER

We investigated 32 specific delusions and 4 delusional characteristics (measured using the Schedules for Clinical Assessment in Neuropsychiatry) and their associations with anger (measured using the Maudsley Assessment of Delusions Schedule). We found 6 delusions and 1 delusional characteristic that were significantly associated with anger after adjustment ( $P<.05$ ), including delusions of being spied on, delusional misidentification, delusions that familiar people are impersonated, delusions of persecution, delusions of conspiracy, threat/control override, and systematized delusions.

### DELUSIONS AND MINOR VIOLENCE

Of the 32 delusions, 6 (including familiar people impersonated, delusions of pregnancy, and delusional lover) were significantly associated with minor violence. These findings (which are available in “Author Table 1,” along with an appendix, from the East London NHS Foundation Trust [[http://www.eastlondon.nhs.uk/rande/archives\\_of\\_general\\_psychiatry\\_-\\_attachements.asp](http://www.eastlondon.nhs.uk/rande/archives_of_general_psychiatry_-_attachements.asp)]) remained significant after controlling for demographic characteristics or comorbid psychopathology. The association between familiar people impersonated and minor violence was attenuated after inclusion of anger due to delusions, but it still remained significant.

Following adjustments, bizarre delusions associated with smell, preoccupation with previous experiences (in-

verse association), and hypochondriacal delusions were significantly associated with minor violence, indicating negative confounding. No specific characteristics of delusions were significantly associated with minor violence, before or after adjustment for demography and comorbid psychopathology. However, when anger due to delusions was included, there was a significant inverse relationship between monothematic delusions and minor violence, indicating negative confounding.

### DELUSIONS AND SERIOUS VIOLENCE

Only 3 delusions demonstrated significant associations with serious violence (see “Author Table 2” from the East London NHS Foundation Trust [[http://www.eastlondon.nhs.uk/rande/archives\\_of\\_general\\_psychiatry\\_-\\_attachements.asp](http://www.eastlondon.nhs.uk/rande/archives_of_general_psychiatry_-_attachements.asp)]), including delusions of being spied on, persecution, and conspiracy. Associations were not confounded by demographic characteristics or psychiatric comorbidity. However, when anger due to delusions was included, these associations were no longer significant.

No characteristics of delusions demonstrated significant associations with serious violence. After inclusion of anger, preoccupation with previous experiences was inversely associated with serious violence, indicating negative confounding.

### ANGER DUE TO DELUSIONS AS MEDIATOR

Anger due to delusions was identified as a potential mediator for 4 delusional beliefs. The relationship between minor violence and the delusion that familiar people are impersonated was significantly, but only partially, mediated by anger ( $z=2.10$ ,  $P=.04$ ). Delusions of being spied on ( $z=3.03$ ,  $P=.002$ ), persecution ( $z=3.09$ ,  $P=.002$ ), and conspiracy ( $z=2.98$ ,  $P=.002$ ) were significantly mediated by anger due to delusions in their relationship with serious violence.

### COMMENT

We found associations between delusions and violent behavior in the year prior to first contact in a large and representative sample of patients with a first episode of psychosis in East London, which contrasts with previous studies.<sup>16,17,20</sup> However, these associations were complex and involved more than 1 pathway. We confirmed strong associations between anger related to delusions and both minor and serious violence. This effect remained significant after controlling for demographic characteristics and comorbid psychopathology typically associated with violence in the general population, which attenuates associations with diagnostic categories of psychosis.<sup>16-18,20</sup> We also ruled out confounding by manic symptoms (which include irritability and anger) and trait anger. The association was stronger for serious violence than for minor violence, and the high attributable risk of anger due to delusions (particularly for serious violence) has implications for preventive intervention and treatment. If anger due to delusions could be identified

and treated, a substantial number of violent incidents could potentially be prevented.

No associations were found between violent behavior and affective states of anxiety, fear, or elation due to delusional beliefs. Depressive affect had a protective effect against both minor and serious violence. This effect has previously been observed.<sup>15</sup> However, when applying the term *protection* in the context of outwardly directed violence, the increased risk of highly adverse outcomes related to depression, such as suicide, must be considered.

Following adjustments, only 6 of 32 delusions resulted in angry affect. These included being spied on, familiar people impersonated, persecution, conspiracy, threat/control override, and misidentification. Delusions of replaced control, sexual, somatic, and other delusions were not associated with anger due to their content. This corresponds to research demonstrating that psychiatric inpatients who report persecutory delusions also report strong negative affect and actions based on these delusions.<sup>22</sup> Furthermore, when delusional beliefs are organized, they provoke anger contrasting with disintegrated delusional systems or monothematic delusions. A subset of delusional beliefs appeared to lead to “tense situations,” which are described as an important component in a causal model of mental illness and violence.<sup>49</sup>

#### PATHWAYS FROM DELUSIONS TO VIOLENT BEHAVIOR

We observed important differences among the effects of specific delusional content on the level of seriousness of violent outcome. Delusions of being spied on, persecutory delusions, and delusions of conspiracy were strong predictors of serious violence even after adjustments. However, when anger due to delusions was included as a covariate, these effects were eliminated. Subsequent mediation analyses revealed that angry affect was the intermediate variable in the pathway from these delusions to serious violence. This is consistent with what would be expected in a causal pathway from delusions to anger to serious violence.

For minor violence, pathways from delusional content to violent outcome appeared to be direct. Delusions of pregnancy and delusional lover both predicted minor violence independently. Familiar people impersonated was significantly associated but partially mediated by anger.

We found few associations between delusions and violent outcome after covariation of additional variables. In confounding/meditational hypotheses, it is typically assumed that statistical adjustment for a third variable will attenuate or eliminate the magnitude of association between predictor and criterion variables. However, it is possible that the removal of a mediator or confounder increases the magnitude of effect, which indicates negative confounding.<sup>50</sup> Such associations included bizarre delusions associated with smell, preoccupation with previous experiences (inverse), hypochondriacal delusions, and monothematic delusions (inverse) predictive of minor violence. An inverse association between preoccupation with previous experiences and serious violence was also found. However, these findings must be interpreted with caution. They could indicate an indirect pathway between

these delusional beliefs/characteristics and violent outcome through other variables, or they may have occurred by chance.

Differences between levels of violence may be a matter of chance, including weapon availability, location on the body of a penetrating injury, or ability of a potential victim to evade injury. However, our findings for serious violence correspond to the notion of intent to inflict more serious harm due to anger as a result of specific delusions. Only a small number of delusions were identified, but their content corresponded to greater threat and potential for retaliatory action. Furthermore, these delusions were highly prevalent. This has implications for future research into anger due to delusions as a risk factor for violence: first, the predictive efficacy of this specific pathway for future violent behavior and, second, whether risk is limited to specific time periods (eg, during first episode) or whether repeated episodes of acute psychosis are accompanied by the same delusional content and anger, corresponding with repeated violence over the course of the illness.<sup>51</sup>

We found a strong relationship between serious violence and delusional content that implied threat (persecutory delusions) but no associations with delusions of replaced control (control override). This may have explained the lack of association with threat/control override, the combination with override cancelling out the otherwise strong association with threat.

Despite earlier descriptions of systematized delusions with themes of jealousy and persecution more prevalent among psychotic offenders detained following serious offending,<sup>1</sup> no positive associations were observed between delusional characteristics and violence, including systematization. However, we did not examine duration of untreated psychosis.<sup>52</sup> Systematization may be important in samples with delusions present for longer periods and specifically after serious violent offending.

#### METHODOLOGICAL CONSIDERATIONS

To our knowledge, this study is among the largest from a single center to ascertain first-episode cases. Moreover, our study was specifically designed to investigate associations between psychosis and violence using robust methods. Furthermore, the comparison of individuals presenting with psychotic symptoms allowed in-depth analyses of features associated with psychopathology.

A wide range of delusions was measured to clarify specific associations with violent outcome. Most importantly, we paid attention to the timing of psychotic symptoms and violent behavior, thereby avoiding confusion between correlations and causal relationships.<sup>53</sup> Nevertheless, our method had limitations in establishing precise temporal associations between these factors. When completing Schedules for Clinical Assessment in Neuropsychiatry ratings, researchers collected data on symptoms 12 months prior to the interview rather than rating symptoms only at the time of the violent incident or over the previous month. Many participants had recently come to the attention of health care services because of their violent behavior, and the clinical researchers had extensive clinical experience with acute psychotic patients prior to research training. Nev-

ertheless, our study included a key weakness inherent in all investigations of causative effects of symptoms on violent behavior: psychotic symptoms can be measured accurately, but the occurrence of associated violence cannot be accurately predicted to study these associations prospectively. Furthermore, we did not include negative symptoms, which are known to decrease risk of violent behavior, or disorganization symptoms, which increase risk.<sup>21</sup> A prospective longitudinal design would be the method of choice to ascertain causal relationships between psychotic symptoms and violence. However, the intervals between follow-up interviews would have to be short, and the interviews administered over a long period, to ensure temporal proximity of presence/absence of symptoms and violent behaviors.

It can be assumed that anger due to delusional beliefs is not dichotomous (as measured in the Maudsley Assessment of Delusions Schedule) but lies on a continuum. A continuous measure of anger related to delusions would both provide greater power to detect associations and allow for assessment of a dose-response relationship between different levels of anger and subsequent violence.

Statistical differentiation between mediation and confounding is not possible. The concepts are equivalent with respect to estimation of effects and standard errors, and the procedures provide no indication of which type of effect is being tested. However, the distinction between mediation and confounding involves directionality and the causal nature of relationships, and these are not determined by statistical testing. Therefore, conceptual considerations such as temporal precedence among variables and the nature of variables must be taken into account.<sup>50</sup> Furthermore, delusions are a foundational part of the illness with deeply rooted causes and do not occur in response to an angry emotion. Therefore, in this context, a mediation model is more plausible.

Acute psychosis may have influenced the subjective judgment of the patients regarding their affective states and interpretation based on contextual cues. This may have constituted additional bias when interviewers and respondents were attempting to assess the violence retrospectively. However, the ratings followed a clinical decision-making process, including all available collateral information, and did not just rely on the self-report of the patients. Nevertheless, not all violent behavior would have been identified, and a tendency toward social desirability may have inhibited some patients from reporting violent incidents.

#### THREAT PROCESSING AND ANGER IN REACTION TO DELUSIONS

Anger is intrinsically and reciprocally related to threat perception and drives violent behavior in the absence of self-regulatory controls.<sup>41</sup> However, studies of cognitive associations between affect and delusions have investigated anxiety more frequently than anger. Evidence for links with anxiety appears strong,<sup>54-57</sup> and anxiety predicts paranoid thoughts<sup>58,59</sup> and persistence of persecutory delusions.<sup>60</sup> Within the threat-anticipation model of paranoid delusions,<sup>61,62</sup> stress and anxiety are thought to arise both from the content of delusions, with further appraisal through worry and rumination. However, fear and anxiety had no

effect on violent outcome in our study and may be more relevant to threat avoidance than violence. Amygdala dysfunction is thought to play a key role in both abnormal emotional perception<sup>63-65</sup> and threat processing.<sup>66</sup> The temporal association with the occurrence of delusions is particularly important in this context because actively paranoid patients are more likely to misidentify neutral facial expressions as angry than those whose symptoms are not active.<sup>67</sup> Reactive aggression is considered the ultimate behavioral expression of anger in response to a threat and involves the amygdala, the hypothalamus, and the periaqueductal gray neural systems.<sup>68</sup> Correspondingly, delusions of persecution, conspiracy, and being spied on, leading to serious violence, would constitute extreme threat (based on misinterpretation of neutral stimuli in the social environment), which then leads to increased responsiveness of these neural systems, whereby the more extreme the reaction of anger, the more serious the violence.<sup>69</sup> Anger due to delusions appeared to constitute the main drive to serious violence. However, no currently available instrument can differentiate between anger due to a delusion and anger as part of the delusion itself. This differentiation would have testable implications for treatment interventions aimed to prevent future violence among deluded patients. If the anger is reactive to the delusional belief, it may be modifiable by treatment that specifically targets the anger. However, if it is part of the delusion itself, this would imply that treatment must simultaneously target the delusion and the associated anger.

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**Online-Only Material:** The eTable is available at <http://www.jamapsych.com>

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