Do cognitive deficits predict negative emotionality and aggression in schizophrenia?

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Abstract
Schizophrenia is associated with an elevated risk of aggression. Cognitive deficits have been associated with inpatient aggression and future violence. The relationship between cognitive deficits and violent behavior has however been inconsistent across studies. In addition, studies have failed to inform how cognitive deficits may contribute to aggression in schizophrenia. The current study examines the association of cognitive deficits with schizophrenia-related aggression and violent offending. It also explored the putative mediating role of negative emotionality on the impact of cognitive deficits on aggression. People with schizophrenia and schizoaffective disorder (N = 78) were recruited from a state hospital. Participants were classified based on their history of violent offending. Participants completed measures of cognition, symptoms, and aggression. Deficits in working memory, reasoning/problem-solving, and verbal learning were the most prioritized for the prediction of violent offending. Participants demonstrated greater impairments in most cognitive domains especially working memory and verbal learning. Offenders also demonstrated greater negative emotionality, excitement/agitation, and incidents of verbal and physical aggression. Negative emotionality and excitement/agitation fully transmitted the effect of cognitive deficits on impulsive aggression in meditational models. Cognitive deficits increase the risk of impulsive aggression in schizophrenia via inefficient regulation of negative affective states.

1. Introduction
From early descriptions of schizophrenia, cognitive impairments have been recognized as one of its core feature (Green and Harvey, 2014). Empirical studies have subsequently established that people with schizophrenia experience impairments in general intellectual ability and specific domains of cognitive functioning (Dickinson et al., 2008; Reilly and Sweeney, 2014). On cognitive tasks, people with schizophrenia often perform in the order of one to two standard deviations below healthy participants (Kern et al., 2011). Cognitive impairments are apparent in all stages of illness and are found in individuals adjudged as high-risk, first episode patients, chronic patients, remitted patients, and unaffected family members (Brewer et al., 2006; Mesholam-Gately et al., 2009; Schulze-Rauschenbach et al., 2015).

Cognitive impairments represent an important treatment target in schizophrenia because along with symptoms, they contribute to significant disability in people with schizophrenia (Juola et al., 2015; Ahmed et al., 2016; Green, 2016). One area of particular disability in people with schizophrenia is in social and interpersonal functioning (Michaels et al., 2014). These deficits encompass difficulties establishing interpersonal relationships, social communication, and managing interpersonal conflicts (Bellack et al., 1989; Bergman and Ericsson, 1996). Interpersonal conflicts are particularly challenging for people with schizophrenia because they contribute to negative emotions in the moments following provocation and persistent negative moods when the individual lacks effective emotion regulation skills (Mitchell and Rossell, 2014; Tully et al., 2014). In extreme cases, negative emotionality leads to maladaptive behaviors such as interpersonal conflicts, substance use, social withdrawal, and impulsive aggression. Indeed people with schizophrenia...
have an elevated risk of impulsive aggression and violent offending that contribute to a poorer clinical picture, longer hospitalizations, relapse, involvement with the criminal justice system, and poorer community reintegration (Broderick et al., 2015; Chang et al., 2015; Knezevic et al., 2015). Schizophrenia is also associated with an elevated risk of victimization particularly when others retaliate in response to aggression by people with schizophrenia (Hodgins et al., 2007).

Studies have linked some of the alterations in cortical structure, function, and connectivity observable in people with schizophrenia to their increased risk of impulsive aggression (Ahmed et al., 2014; Hoptman, 2015; Hoptman and Ahmed, 2016; Soyka, 2011). For example, prefrontal deficits contribute to elevated negative emotionality, poor decision-making, action selection, and response disinhibition (Serper et al., 2008). Given that frontal impairments known to be prevalent among people with schizophrenia may also contribute to their risk of aggression, there is interest in whether cognitive deficits—particularly indicators of frontal dysfunction—may reliably predict aggressive tendencies.

The identification of cognitive functions that predict impulsive aggression informs the search for neural substrates that underlie impulsive aggression. Some studies have examined the cognitive functioning of schizophrenia patients with a history of violence relative to patients without a history of violence (see Table A1 in the supplement). The results of these studies have been mixed with several published studies suggesting that patients with a history of aggression perform worse on cognitive tasks (Barkataki et al., 2005; Fullam and Dolan, 2008; Hanlon et al., 2012), whereas others find no differences (Chung et al., 2010; Lafayette et al., 2003; Silver et al., 2005). Still others found that violent patients performed better on cognitive tasks than non-violent patients (Rasmussen et al., 1995). A recent meta-analysis (Reinharth et al., 2014) obtained small average effect size differences between violent and non-violent patients on global cognition, insight, motor functioning, memory, attention, processing speed, and visual-spatial reasoning with violent patients scoring lower. Social cognition deficits—which refer to cognitive abilities deployed in social situations to aid in perceiving, interpreting, and responding to others’ behavior—also contribute to violence in schizophrenia and seem to more proximally contribute to aggression than other cognitive variables (O’Reilly et al., 2015; Penn et al., 1996).

The cause of inconsistencies in the association between cognitive functioning and violent offending across studies is subject to speculation. Differences in diagnostic composition of study samples may explain some of the discrepancies. It seems that violent schizophrenia patients with a history of childhood antisocial behavior—which may serve as a precursor to violence and other forms of antisocial behavior—are less cognitively impaired than nonviolent patients with schizophrenia (Naudts and Hodgins, 2006). Violent patients appear more impaired when samples do not have a childhood history of conduct problems. Relatedly, differences in the operationalization of aggression—that is, whether impulsive/reactive aggression or premeditated/instrumental aggression is measured—may explain inconsistencies across studies. Studies that have found cognitive differences between violent and non-violent patients have failed to illuminate how cognitive dysfunction may contribute to impulsive aggression. Overlap in neural circuitry implicated in emotion regulation abnormalities, impulsivity, and impulsive aggression (Etkin et al., 2015; Hoptman et al., 2010, 2014) suggests that emotion regulation deficits that lead to increased baseline negative emotionality may be a precursor to impulsive aggression and perhaps a mediator of any associations between cognitive deficits and impulsive aggression.

The goal of the current study was to determine if there are any patterns of cognitive deficits that predict violent offender status and impulsive aggression in an inpatient sample of people with schizophrenia and schizoaffective disorder. The study 1) used multivariate statistical models to identify cognitive patterns that may distinguish violent offenders from non-offenders hospitalized in a state hospital; 2) examined the association of cognitive domain scores with incidences and types of aggression; and 3) examined the putative intervening role of negative emotionality on the effect of cognitive impairments on impulsive aggression. It was primarily postulated that differential patterns of cognitive impairments will distinguish violent offenders with schizophrenia. It was further postulated that general intellectual ability and cognitive domains will predict the frequency of aggressive incidents. Finally, it was also hypothesized that negative emotionality will mediate the association of cognitive functions with impulsive aggression in the hospital sample.

2. Method

2.1. Participants

The study recruited participants from East Central Regional Hospital (ECRH) in Augusta, Georgia from October 8, 2011 to June 30, 2014. Participants were people with schizophrenia or schizoaffective disorder that had been enrolled in the hospital’s cognitive training program and consented prior to beginning cognitive remediation groups in the forensic and mental health units. The study sample comprised 78 long-term hospitalized individuals with persistent psychotic symptoms and limited community placement options. A subset of the sample were 43 individuals with a history of violent offending who at a certain point had been rendered to the custody of the department of human resources following the completion of a violent offense. Violent offenses in the sample encapsulated domestic violence, assault and battery, threat of injury to another, sexual assault, rape, harassment, armed robbery, and homicide.

After unit-based treatment teams referred patients to the hospital’s cognitive training program, participants were recruited to participate in a clinical study of cognitive remediation. Participants who consented to participate in the cognitive remediation study were then extensively characterized using a battery of measures at baseline (discussed below). The eligibility criteria for the baseline measurement study were:

1. Participants had to have a clinical diagnosis of schizophrenia or schizoaffective disorder;
2. Participants were 18-years-old or older;
3. No evidence of neurological disorders, developmental disabilities, head trauma;
4. No reported history childhood antisocial behaviors or an Axis II personality disorder diagnosis;
5. Participants were English speaking.

The Structured Clinical Interview for DSM-IV [SCID; (First et al., 1997)] served to establish participants’ clinical diagnosis and assess substance use history. The parent cognitive remediation study was approved by the Institutional Review Boards of the Medical College of Georgia in Augusta University and the Georgia Department of Public Health. Participants were evaluated for their decisional capacity to consent to study and participants adjudged as having decisional capacity provided full written informed consent.

2.2. Measures

2.2.1. Demographic and clinical characteristics data

A standard demographic and clinical characteristics form was used to obtain demographic information including age, sex, race/ethnicity, and education level. Clinical characteristics such as medications, hospitalization tenure, hospitalization and legal history were obtained from a review of the hospital charts and recorded in the demographic and clinical characteristics form.

2.2.1.1. Aggression history. The assessment of aggression history is part of a standard assessment for participants enrolled in the services at
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