Published in final edited form as:

Psychiatry Res Neuroimaging. 2019 May 30; 287: 60–62. doi:10.1016/j.psychres.2019.04.003.

Amygdalar Volume and Violent Ideation in a Sample at Clinical High-Risk for Psychosis

Xinyang Feng, MS, Frank Provenzano, PhD, Paul S. Appelbaum, MD, Michael D. Masucci, MA, Gary Brucato, PhD, Jeffrey A. Lieberman, MD, and Ragy R. Girgis, MD

Columbia University, Department of Psychiatry, New York State Psychiatric Institute (NYSPI), New York, New York, USA

Abstract

We previously demonstrated that violent ideation predicts both violent acts and eventual progression to syndromal psychosis in individuals at clinical high-risk for psychosis (CHR). We performed amygdalar surface morphometry analysis on MRI scans from 70 CHR individuals, 21 of whom had violent ideation, 49 of whom did not. CHR individuals with violent ideation have abnormal and asymmetric amygdalar volumes. These data suggest some commonalities in the genesis of violence and aggression among clinical populations, as well as that there may be specific neurobiological links between violence and psychosis.

Keywords

violence; ideation; psychosis; clinical high-risk; amygdala; MRI

1. Introduction

We recently reported that in a longitudinal study of 200 adolescents and young adults at clinical high-risk for psychosis (CHR) violent behavior and violent ideation at baseline strongly predicted transition to syndromal psychosis as well as outcome violent behavior within an average of one week following transition to syndromal psychosis (Brucato et al., 2018). The violent ideation was often experienced as intrusive and ego-dystonic, occurring in one-third of participants (Brucato et al., In Press). The content of this ideation was typically found to be severe in nature, involving physical harm to others using one's body or a weapon, and was associated with higher suspiciousness and overall positive symptoms. These results support the conclusion that violent thoughts of this type may be linked to the phenomenology of attenuated psychosis, analogous to suicidal thoughts in depression.

Corresponding Author: Ragy R. Girgis, MD; 1051 Riverside Drive, Unit 31, New York, NY 10032 (ragy.girgis@nyspi.columbia.edu) 646 774 5553; fax 646 774 5237.

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.

Because of the amygdala's role in fear learning and memory, previous studies have suggested that smaller amygdalar volumes are associated with higher levels of aggression and violence (Johansen et al., 2011; Rosell and Siever, 2015). Studies examining amygdalar activity have also implicated the amygdala in aggression/violence (Rosell and Siever, 2015). Abnormalities in connectivity between the amygdala and prefrontal cortices have been suggested to mediate the behavioral manifestations of these amygdalar abnormalities (Hoptman et al., 2010). However, no studies have examined the neurobiology of violence in CHR samples, hence we undertook the following analysis in our CHR cohort. (For a full description of the methodology, see Brucato et al (Brucato et al., 2018; Brucato et al., 2019)).

2. Methods

Participants were help-seeking CHR outpatients, aged 13–30, enrolled in the Center of Prevention and Evaluation (COPE) at the New York State Psychiatric Institute (NYSPI) of Columbia University's Department of Psychiatry. The authors affirm that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human subjects/patients were approved by the NYSPI IRB. All participants met criteria for the Attenuated Positive Symptom Syndrome (APSS) defined in the Structured Interview for Psychosis-Risk Syndromes (SIPS). Symptoms were not better explained by any other DSM disorder or substance use. All subjects over 18 years provided written informed consent; minors provided assent with written consent by a parent or legal guardian.

Information about violent ideation at the time of enrollment in COPE was assessed with the SIPS, the clinical interview, and collateral information from prior records, family members and referral sources. Violent ideation was defined based on the categories established in the MacArthur Community Violence Interview (Steadman et al., 1998) as previously described (Brucato et al., 2018).

For the current analysis, we included individuals from a longitudinal study of CHR subjects (Brucato et al., 2018) who underwent a T1-weighted structural MRI (N=70) as part of a concurrent longitudinal brain imaging study of CHR individuals (R01MH093398). We performed amygdalar surface morphometry analysis using SPHARM-PDM (spherical harmonic point distribution models) (Schobel et al., 2013; Styner et al., 2006). Specifically, we segmented the amygdala from T1-weighted structural MRI using FreeSurfer (<http://freesurfer.net>). The amygdala segmentation masks were processed through the SPHARM-PDM pipeline to generate aligned amygdalar surfaces across subjects. All structural images run through FreeSurfer were examined and corrected by a trained reviewer for poor segmentation and other artifacts. We performed scaling normalization using each subject's intra-cranial volume (ICV) to correct for head size. The average surface of the two within-group average surfaces was used as the template.

At each vertex, the signed magnitude of the local difference vector projected onto the template surface normal vector was used to measure the local volume variation. We

performed vertex-wise linear regression with the presence of violent ideation as the testing variable, using gender and age as covariates. Significance was defined as $p < 0.05$ and cluster vertex size > 10 . We employed heuristic statistical thresholds for contiguous significant vertices (number of vertices ≥ 10 , uncorrected $p < 0.05$), similar to the practice setting contrast and extent thresholds in statistical parametric mapping in voxel space.

3. Results

3.1. Demographic and Clinical Information

We obtained baseline imaging on a total of 70 CHR individuals, including 21 who had violent ideation (VI) and 49 who did not have violent ideation (non-VI). The demographic characteristics of the groups were similar (Gender: non-VI 31 male, 18 female; VI 15 male 6 female; Age mean (SD): non-VI 21.57 (3.76), VI 20.52 (3.60); Ethnicity: non-VI 16 Hispanic, 33 non-Hispanic; VI 7 Hispanic, 14 non-Hispanic; Race: non-VI 24 Caucasian, 9 African American, 1 Asian, 15 Mixed; VI 9 Caucasian, 5 African American, 2 Asian, 5 Mixed). As expected, individuals with violent ideation had greater symptomatology as measured by the SIPS (mean (SD): Total Positive Symptoms: non-VI 13.49 (4.69), VI 16.24 (2.49), $p = 0.014$; Total Negative Symptoms: non-VI 17.12 (6.15), VI 18.95 (5.97), $p = 0.254$; Total Disorganization Symptoms: non-VI 9.47 (3.39), VI 12.24 (3.11), $p = 0.002$; Total General Symptoms: non-VI 11.02 (4.29), VI 13.10 (4.04), $p = 0.064$). This was only significant for Total Positive and Disorganization symptoms.

3.2. Morphometry Results

The amygdalar morphometry results are shown in the Figure 1. We observed different patterns in the left and right amygdala. The right amygdala shows a region of decreased volume in the vicinity of the basal nucleus in the group with violent ideation, whereas the left amygdala shows a region of increased volume in the vicinity of the inferior lateral nucleus in the group with violent ideation. No significant relationships were observed between amygdalar morphometry and other clinical measures.

4. Discussion

We previously demonstrated that violent ideation, often experienced as ego-dystonic in nature, is relatively common in CHR individuals, is related to suspiciousness and positive symptoms in general, and predicts both violent acts and eventual progression to syndromal psychosis. These results suggest phenomenological links between violence and early psychosis, and that checking for violent thoughts in CHR individuals is important (Brucato et al., 2018; Brucato et al., 2019).

In the current study, we extend these clinical observations by reporting neurobiological correlates of violent ideation in CHR individuals. In particular, CHR individuals with violent ideation have abnormal and asymmetric amygdalar volumes. The presence of abnormal and lateralized amygdalar volumes in CHR individuals with violent ideation is consistent with the literature on the neurobiology of violence and aggression (Rosell and Siever, 2015), while the nature of the abnormalities is unique. These data suggest some commonalities in the genesis of violence and aggression among clinical populations, as well as that there may

be specific neurobiological links between violence and psychosis. Therefore, it may be possible to develop a neurobiological marker of predisposition, or risk, for violence that can be used in addition to clinical risk factors, such as substance use or history of antisocial behavior. These data also suggest that it may be possible to develop biological or somatic-based treatments, such as medications, aimed at decreasing violence in individuals with psychotic disorders, and that single-subject amygdalar morphometry may be a viable measure of target engagement for such treatment development. Therefore, further research into the neurobiology of violent ideation and behavior in psychosis is warranted.

Acknowledgments

Funding: This project was supported by National Institute of Mental Health grant R01MH093398 and by the New York State Office of Mental Hygiene.

Role of the Funder/Sponsor: The sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Declaration of Interest

R. Girgis acknowledges receiving research support from Otsuka, Allergan/Forest, BioAvantex, and Genentech. J. Lieberman has received support administered through his institution in the form of funding or medication supplies for investigator-initiated research from Lilly, Denovo, Biomarin, Novartis, Taisho, Teva, Alkermes, and Boehringer Ingelheim, and is a member of the advisory board of Intracellular Therapies and Pierre Fabre. He neither accepts nor receives any personal financial remuneration for consulting, advisory board or research activities. He holds a patent from Repligen and receives royalty payments from “SHRINKS: The Untold Story of Psychiatry.” F. Provenzano is an advisor for and holds equity in Imij Technologies. No other authors have disclosures.

References

- Brucato G, Appelbaum PS, Lieberman JA, Wall MM, Feng T, Masucci MD, Altschuler R, Girgis RR, 2018 A Longitudinal Study of Violent Behavior in a Psychosis-Risk Cohort. *Neuropsychopharmacology* 43, 264–271. [PubMed: 28745307]
- Brucato G, Appelbaum PS, Masucci MD, Rolin S, Wall MM, Levin M, Altschuler R, First MB, Lieberman JA, Girgis RR, 2019 Prevalence and phenomenology of violent ideation and behavior among 200 young people at clinical high-risk for psychosis: an emerging model of violence and psychotic illness. *Neuropsychopharmacology* 44, 907–914. [PubMed: 30591713]
- Brucato G, Appelbaum PS, Masucci MD, Rolin S, Wall MM, Levin M, Altschuler R, First MB, Lieberman JA, Girgis RR, In Press. Prevalence and phenomenology of violent ideation and behavior among 200 young people at clinical high-risk for psychosis: An emerging model of violence and psychotic illness. *Neuropsychopharmacology*.
- Hoptman MJ, D’Angelo D, Catalano D, Mauro CJ, Shehzad ZE, Kelly AM, Castellanos FX, Javitt DC, Milham MP, 2010 Amygdalofrontal functional disconnectivity and aggression in schizophrenia. *Schizophr Bull* 36, 1020–1028. [PubMed: 19336392]
- Johansen JP, Cain CK, Ostroff LE, LeDoux JE, 2011 Molecular mechanisms of fear learning and memory. *Cell* 147, 509–524. [PubMed: 22036561]
- Rosell DR, Siever LJ, 2015 The neurobiology of aggression and violence. *CNS Spectr* 20, 254–279. [PubMed: 25936249]
- Schobel SA, Chaudhury NH, Khan UA, Paniagua B, Styner MA, Asllani I, Inbar BP, Corcoran CM, Lieberman JA, Moore H, Small SA, 2013 Imaging patients with psychosis and a mouse model establishes a spreading pattern of hippocampal dysfunction and implicates glutamate as a driver. *Neuron* 78, 81–93. [PubMed: 23583108]
- Steadman HJ, Mulvey EP, Monahan J, Robbins PC, Appelbaum PS, Grisso T, Roth LH, Silver E, 1998 Violence by people discharged from acute psychiatric inpatient facilities and by others in the same neighborhoods. *Arch Gen Psychiatry* 55, 393–401. [PubMed: 9596041]

Styner M, Oguz I, Xu S, Brechbuhler C, Pantazis D, Levitt JJ, Shenton ME, Gerig G, 2006 Framework for the Statistical Shape Analysis of Brain Structures using SPHARM-PDM. *Insight J*, 242–250. [PubMed: 21941375]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Highlights

- We performed amygdalar surface morphometry analysis on MRI scans from 70 CHR individuals, 21 of whom had violent ideation, 49 of whom did not.
- CHR individuals with violent ideation have abnormal and asymmetric amygdalar volumes.
- These data suggest some commonalities in the genesis of violence and aggression among clinical populations, as well as that there may be specific neurobiological links between violence and psychosis.

Figure 1.

The amygdala surface morphometry results. (A) The t-values for the regression analyses are rendered on the surface. Red indicates that the group with violent ideation (VI) has greater volume, and blue indicates that the group with violent ideation has less volume. Note the anterior side of the surface has no significant clusters and thus is not shown here. (B) The measures extracted from the suprathreshold ($p < 0.05$) cluster residualizing gender and age are plotted to show the individualized morphometric measures.