



Source-Based Morphometry Reveals Gray Matter Differences Related to Suicidal Behavior in Criminal Offenders

Carla L. Harenski, PhD¹, Keith A. Harenski, BS¹, Vince D. Calhoun, PhD^{1,2}, and Kent A. Kiehl, PhD^{1,2}

¹The Mind Research Network and Lovelace Biomedical and Environmental Research Institute, Albuquerque, NM

²University of New Mexico, Albuquerque, NM

Abstract

Relative to the general population, criminal offenders have a higher risk of suicide. Neurobiological deficits related to suicidal behavior have been identified in the general population, but unexamined in offenders to date. We examined the association between brain morphology and suicidal behavior in adult male criminal offenders. Brain morphology was examined using voxel-based morphometry (VBM) and source-based morphometry (SBM), a multivariate alternative to VBM which analyzes brain volume in between-subject spatially independent networks. Results showed that offenders with past suicide attempts ($n = 19$), relative to offenders without past suicide attempts ($n = 19$) and non-offenders ($n = 26$), had reduced gray matter in an SBM component that comprised the posterior cingulate, dorsal prefrontal cortex, and amygdala. The SBM source weights were significantly associated with suicide attempts independent of other suicide risk variables (e.g., depression). VBM results were similar to the SBM results but less robust. The results reveal a potential neurobiological marker of vulnerability to suicidal behavior among criminal offenders and illustrate the utility of multivariate methods of gray matter analyses.

Keywords

Suicide; Criminal; Neuroimaging; Gray matter; Posterior cingulate

Introduction

More than 800,000 people die by suicide each year (Zalsman et al., 2016). Several risk variables for suicide have been identified, including early childhood abuse, impulsivity, aggression, psychiatric disorder, and substance abuse (Brown et al. 2000; Dube et al. 2001;

Correspondence to: Carla L. Harenski, The Mind Research Network, 1101 Yale Blvd NE, Albuquerque, NM 87106, 505-272-5684, charenski@mrn.org.

Compliance with ethical standards

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare that they have no conflict of interest.

Arsenault-Lapierre et al. 2004; Swann et al. 2005; Nock and Kessler 2006). Studies have also begun to identify neural correlates of suicidal behavior (Ding et al., 2015; Renteria et al., 2017; Johnston et al., 2017; Duarte et al., 2017). Neuroimaging measures may add predictive value to clinical suicide risk variables, as they do not depend on self-report data and/or subjective clinical assessments.

Neuroimaging studies in non-offenders have linked several cortical and subcortical regions to suicidal behavior. Mood disorder patients with a history of suicidal behavior have showed volume reductions in the dorsal, orbitofrontal, and ventrolateral prefrontal cortex, relative to patients without a history of suicidal behavior. Results in other frontal regions, such as the anterior cingulate (ACC) has been mixed (Hwang et al., 2010; Wagner et al., 2011; Ding et al., 2015; Duarte et al., 2017). Studies have also reported associations between regional brain volumes and specific features of suicidal behavior. For example, dorsal prefrontal volume was correlated with lethality of suicidal act and number of suicidal acts (Ding et al., 2015). A meta-analysis of anatomical and functional imaging studies identified the medial orbitofrontal cortex (OFC), left caudate, left posterior superior temporal gyrus (pSTG), anterior cingulate (ACC), and posterior cingulate (PCC) as regions showing aberrant structure or activity in suicidal individuals across studies (van Heeringen et al., 2014). However, the latter findings are potentially complicated by the combining of results across different imaging modalities (a recent meta-analysis focusing on voxel-based morphometry results did not replicate the findings; see Renteria et al., 2017). Studies have also shown increased activation in several of these regions to emotional stimuli, such as facial expressions (Jollant et al. 2008; Pan et al. 2013), and reduced gray matter volume in OFC and other prefrontal regions implicated in decision making and behavioral control (Aguilar et al. 2008; Monkul et al. 2007; Benedetti et al. 2011), in suicide attempters relative to non-attempters. Inverse correlations between OFC volume and rostral ACC and left caudate activation have been reported in depressed individuals during facial emotion recognition (Scheuerecker et al. 2010; Wagner et al. 2008). The latter studies have not been conducted in suicidal individuals, but the above evidence suggests that suicidal behavior may be related to prefrontal – limbic dysfunction that affects the ability to regulate emotion and behavior. To date, however, published studies have more consistently implicated prefrontal regions in suicidal behavior. Evidence for limbic region involvement is less conclusive.

While several individual brain regions have been implicated in suicidal behavior, whether some of these regions form naturally grouped circuits which show differences between suicidal and non-suicidal individuals has not previously been studied. As a complement to individual region of interest approaches, studying group differences at the circuit level can promote understanding of how altered relationships between regions may inform suicidal behavior. To investigate this, we used source-based morphometry (SBM) to examine gray matter volume within neural networks and group differences in suicidal behavior. SBM is used to separate gray matter volume into maximally independent source networks. It is a data driven, multivariate analysis technique which uses spatial information between voxels to identify independent grouped “sources”, i.e. spatially distinct sets of brain regions in which gray matter covaries between individuals (Xu et al. 2009). An advantage of SBM over univariate approaches, such as voxel-based morphometry (VBM), is that SBM uses independent components analysis (ICA) to identify sets of voxels that have similar variance

patterns (components), and the component values (i.e., loading coefficients, which represent the average brain volume across each component, after accounting for the other components) which are compared across groups. This greatly reduces the severity of multiple comparison correction (i.e., correcting for every voxel in the brain) while also providing meaningful information about voxel patterns. Studies in certain clinical populations, such as schizophrenia, have shown that SBM revealed gray matter volume differences that were not identified by VBM (Xu et al. 2009; Kašpárek et al. 2010; Wolf et al. 2014).

Another advantage of SBM is that it does not require defining a priori regions of interest, which was desirable in the present study for two reasons. First, the results of prior brain imaging studies of suicidal behavior are mixed and do not point to a consistent set of implicated brain regions/networks. Second, the current study specifically examined incarcerated criminal offenders. To date, the neural correlates of suicidal behavior in criminal offenders have not been studied. Males who become imprisoned at some point show increased suicidal thoughts and behaviors throughout their lives, with a rate almost six times the general population (Fruehwald et al. 2004; Jenkins et al. 2005). While the clinical risk variables for suicidal behavior mentioned above overlap with those identified in non-offender samples (Blaauw et al. 2005; Douglas et al. 2008; Swogger et al. 2011), whether the results of neuroimaging studies in suicidal non-offenders extend to offenders is unknown. The lack of prior neuroimaging research in criminal offenders with suicidal tendencies is in part due to incarceration and the practical challenges associated with bringing imaging capabilities to prisons (or transporting prisoners to outside imaging facilities, which is often not possible or permissible). We used a unique mobile MRI scanner that was situated on prison grounds, enabling us to recruit and scan incarcerated offenders and analyze their imaging data using SBM. We also analyzed brain volume within individual regions using voxel-based morphometry (VBM), to compare the results with prior published studies of suicidal behavior in non-offenders.

In summary, we examined gray matter volume using SBM and VBM in criminal offenders with a history of suicide attempt/s, criminal offenders with no history of suicide attempts, and non-offenders. Although not all suicide attempters go on to complete suicide, past attempts are among the strongest predictors of future suicide (Gunnell and Lewis 2005). We hypothesized that: 1) SBM would reveal one or more components (i.e., sources), comprising prefrontal and limbic regions involved in emotion processing and regulation and previously implicated in suicidal behavior in non-criminal offenders, e.g., OFC, ACC, PCC), 2) Gray matter volume in the relevant source/s would be reduced in criminal offenders with a history of suicide attempts relative to those without prior suicide attempts and non-offenders. We also examined, but did not generate specific hypotheses regarding, gray matter volume within each region previously implicated in the suicidal behavior in non-offenders: dPFC, OFC, ACC, left caudate, left pSTG, and PCC.

We also examined clinical variables related to suicide risk in criminal offenders including early childhood abuse, impulsivity, aggression, comorbid psychiatric disorder, and substance abuse. We hypothesized that reduced prefrontal-limbic gray matter volume would be significantly related to suicidal behavior beyond the effects of these variables.

Method

Participants

The total sample included 65 participants: incarcerated male criminal offenders with ($n = 19$) and without ($n = 19$) a history of suicide attempts, and male community non-offenders ($n = 27$). The offender groups were generated from a larger database of incarcerated offenders that was filtered to select those with suicide attempts and a matched (age, race/ethnicity, IQ) group of offenders without suicide attempts. Offenders were recruited from medium-security state prison facilities in New Mexico. Non-offenders were recruited from the Albuquerque, NM community. Inclusion criteria were: 1) age between 18 and 60, 2) native English speaker, 3) estimated IQ 70 or higher, 4) reading level 4th grade or higher, 5) no history of epilepsy or seizures, 6) no major medical illness (e.g., HIV), 7) no lifetime psychotic disorder in self or first-degree relative, 8) no current major mood or anxiety DSM-IV Axis I disorder. Community non-offenders were additionally required to have no history of drug use or alcohol use disorder and no criminal offenses. Written informed consent was obtained from all participants at the initial study session after a complete description of the study procedures, which were approved by the University of New Mexico Institutional Review Board. Participants were paid at a rate commensurate to work assignments at their facility.

Suicidal behavior was defined based on criteria from the Columbia Suicide Severity Rating Scale (C-SSRS)(Posner et al. 2011): a potentially self-injurious act committed with at least some wish to die as a result of the act. Relevant life history details were obtained via interviews including the Structured Clinical Interview for DSM-IV Disorders (SCID-IV) and Hare Psychopathy Checklist-Revised (PCL-R) interviews (see below), and review of institutional files that contained psychosocial history summaries including past suicidal behavior. The demographic characteristics of the three groups are provided in Table 1.

Clinical Assessments

Past and present DSM-IV Axis I and II disorders were evaluated in all participants using the research version of the Structured Clinical Interview for DSM-IV Disorders (SCID-IV) (First 1997). Intelligence was estimated using the vocabulary and matrix reasoning subtests of the Wechsler Adult Intelligence Scale (WAIS) (Wechsler 1997; Ryan 1999). Psychopathy was assessed using the Hare Psychopathy Checklist-Revised (PCL-R) (Hare 2003). Although psychopathy was not a focus of the present study, the PCL-R includes questions about suicidal behavior and was used to help determine whether participants had previously attempted suicide.

We also assessed clinical variables that are related to suicidal behavior in criminal offenders. History of depression and substance use disorder (i.e., abuse or dependence) were evaluated with the SCID. We did not evaluate other psychiatric conditions associated with suicide risk, such as schizophrenia, because the participants were taking part in a larger study in which history of a psychotic disorder was an exclusion criterion that was determined during initial screening. Impulsivity was measured using the Barratt Impulsiveness Scale (Patton 1995). Early abuse was assessed using the Detailed Assessment of Post-Traumatic Stress (Briere

and Elliott 2003). For ten participants who did not complete the DAPS (five from the suicide attempt group), information was obtained from the PCL-R. Both assessments include a question about whether the individual had experienced physical or sexual abuse from a parent or other caretaker during childhood. For history of aggressive behavior, participants were assigned to one of two categories: no aggression or minor aggression (e.g., assault without injury or weapon use) and serious aggression (e.g., sexual offense, homicide) (Swanson et al. 2006). Violence information was obtained via an interview in which participants were asked if they had ever committed each of several different classes of crime (e.g., robbery, homicide, DUI, minor assault). Self-report was checked against file/criminal records.

Other Participant Characteristics

Offenders had a history of various crimes including drug offenses (five suicide attempters and six non-attempters), theft or robbery (six attempters and nine non-attempters), assault (four attempters and four non-attempters), sexual assault (two attempters and three non-attempters), and murder (two attempters and two non-attempters).

Most offenders had no history of head injury ($n = 16$) or a head injury with no loss of consciousness (LOC) ($n = 6$). Five of the remaining participants had a prior head injury with LOC longer than 15 minutes. Seven had a head injury with LOC less than 5 minutes. LOC data was not available for one participant. Neither the incidence of head injury ($\chi^2(1) = 0.65, p = 0.42$), nor the total time LOC ($t(34) = 0.03, p = 0.97$) significantly differed between suicide attempters and non-attempters.

Most offenders ($n = 26$) met DSM-IV criteria for antisocial personality disorder. ASPD rates did not differ significantly between suicide attempters and non-attempters ($\chi^2(1) = 0.49, p = 0.48$). Total psychopathy (PCL-R) scores also did not differ significantly between attempters and non-attempters ($t(34) = 0.12, p = 0.90$).

MRI Acquisition

High-resolution T1-weighted structural MRI scans were collected on a Siemens 1.5T Avanto mobile scanner, stationed at the correctional facility, using a multi-echo MPRAGE pulse sequence (repetition time = 2530 ms, echo times = 1.64 ms, 3.50 ms, 5.36 ms, 7.22 ms, inversion time = 1100 ms, flip angle = 7° , slice thickness = 1.3 mm, matrix size = 256×256) yielding 128 sagittal slices with an in-plane resolution of $1.0 \text{ mm} \times 1.0 \text{ mm}$. Data were preprocessed and analyzed using the Statistical Parametric Mapping software (SPM12; <http://www.fil.ion.ucl.ac.uk/spm>). T1 images were manually inspected by an operator blind to subject identity and realigned to ensure proper spatial normalization. Data were then spatially normalized into the standard Montreal Neurological Institute (MNI) space, resampled to $2 \times 2 \times 2 \text{ mm}$ voxels and segmented into white matter, gray matter and cerebrospinal fluid. The segmented maps were modulated to preserve total cerebral volume (Ashburner and Friston 2005) and voxels with values less than 0.15 were removed. The segmented images were then smoothed using a Gaussian kernel with a full-width at half-maximum (FWHM) of 10 mm.

All MRI scans were reviewed by a licensed neuroradiologist. One of the 65 participants had a clinically significant finding resulting in a routine referral. The subject was in the suicidal behavior group and had no history of head injury.

Source-Based Morphometry Analysis

The SBM analysis methods have been described in detail elsewhere (Xu et al., 2009). Following preprocessing, the Group ICA fMRI Toolbox (GIFT) software (<http://mialab.mrn.org/software/gift>) was used to calculate the number of maximally independent components using a modified minimum description length (MDL) method (Li et al. 2007) in all 64 subjects. Next, independent component analysis (ICA) was performed using the Infomax algorithm. Each gray matter image was converted into a one dimensional vector, and arrayed into a 64 (subjects) row by gray matter matrix. The matrix was then decomposed into a mixing matrix (subjects by components) and source matrix (components by voxels). Group differences (offenders with suicide attempts, offenders with no suicide attempts, non-offenders) in each column of the mixing matrix were analyzed in MATLAB (Version 7.12.0, 2011; MathWorks, Natick, MA, USA) using ANOVA ($p < 0.05$, Bonferroni-corrected for multiple comparisons (i.e., number of components)) with age, IQ estimate, and total brain volume (TBV; i.e., GMV + WMV) included as covariates. Post-hoc group comparisons ($p < 0.05$, Bonferroni-corrected for multiple comparisons (i.e., number of groups) were analyzed in SPSS (Version 23, SPSS inc.; www.spss.com).

Voxel-Based Morphometry Analysis

The same preprocessed images used in the SBM analysis were entered into a three-group ANOVA in SPM12 to identify voxels that showed significant gray matter differences across groups ($p < 0.05$, FWE whole-brain corrected). Age, IQ estimate, and TBV were included as covariates. For comparison with prior studies, regions of interest including (dorsal prefrontal cortex (BA 8), medial OFC, ACC, PCC, left caudate and left pSTG) were examined at a less conservative threshold, $p < 0.005$, uncorrected, followed by correction for multiple comparisons within each region ($p < .05$, FWE small-volume corrected (SVC)). We also examined the amygdala, which was not hypothesized a priori but is part of the prefrontal- limbic circuit and was implicated in suicidal behavior in the SBM analysis. For all ROIs, image masks obtained from the Wake Forest University Pick Atlas Toolbox in SPM12 based on automated anatomical labeling (AAL) were used for the SVC.

Results

Clinical Variables and Suicide Attempts in Criminal Offenders

Zero-order regressions evaluating suicide attempt history (yes/no) based on depression, alcohol use disorder¹, early abuse, impulsivity and aggression are shown in Table 2. None of these variables were significantly related to suicide attempt history.

¹Drug use disorder could not be analyzed due to (quasi) separation: nearly all participants ($n = 34$) met criteria for a drug use disorder. C29 loading weights were not significantly different between offenders with and without a drug use disorder ($t(36) = 1.44$, $p = 0.16$)

Group Differences in Gray Matter Source Volumes (SBM)

The ICA analysis generated 30 independent components. Eight of these components were determined to be artifacts (e.g., motion related) based on the criteria defined by Xu et al (2009): components containing several sharp edges near the boundary of the brain or appearing primarily in regions that do not contain gray matter (e.g., white matter or ventricles). These components were excluded from subsequent analysis. The ANCOVA results revealed a main effect of group in one source (C29) ($F_{(2,64)} = 7.76, p = 0.001$), which survived Bonferroni correction for multiple comparisons (22 components, $p = 0.022$). C29 comprised several cortical and subcortical regions including the PCC/precuneus, superior and lateral prefrontal cortex, inferior parietal cortex, amygdala, insula, superior occipital gyrus, cuneus, and cerebellum (Figure 1, Table 3). Post hoc tests (with Bonferroni correction) indicated that C29 loading weights were significantly lower in offenders with a history of suicide attempts compared to offenders with no prior attempts ($p = 0.003$) and non-offenders ($p = 0.006$). The difference between non-attempters and non-offenders was not significant ($p = 0.99$).

The ANCOVA results remained significant when the participant with a clinically significant MRI finding was excluded from the analysis ($F_{(2,63)} = 9.24, p < 0.001$).

Significance of SBM Source Relative to Other Risk Variables

We used hierarchical logistic regression to examine the association between C29 loading weights and suicide attempt history beyond the effects of clinical variables (i.e., depression, early abuse, impulsivity, alcohol use disorder, and aggression; Table 2). The results showed that, after including the clinical variables in the model, lower C29 loading weights continued to be significantly associated with an increased likelihood of a past suicide attempt, ($\beta = -0.91, SE(\beta) = 0.46, p = 0.05, OR/95\% CI: 0.40(0.16 - 1.00)$).

Group Differences in Gray Matter Regional Volumes (VBM)

A main effect of group was present in the PCC ($x = 3, y = -45, z = 16, k = 760, F_{(2.59)} = 14.83, p = 0.001$, small-volume corrected). PCC volumes were significantly lower in offenders with a history of suicide attempts compared to offenders with no prior attempts ($p < 0.001$). The group difference between suicidal offenders and non-offenders was not significant ($p = 0.11$). No significant group differences in any other regions were found.

Discussion

This study tested the hypothesis that gray matter volume in prefrontal-limbic networks is related to suicidal behavior in criminal offenders. Using a multivariate SBM analysis, we found that offenders with a history of suicide attempts, relative to offenders with no suicide attempts and non-offenders, had significantly less gray matter in a network comprising prefrontal and parietal regions, including the posterior cingulate/precuneus and dorsal prefrontal cortex, as well as the inferior parietal cortex, amygdala, insula, superior occipital gyrus, cuneus, and cerebellum. This group difference was significant beyond the effects of other suicide risk variables. The VBM results in PCC were consistent with the SBM results but less robust (e.g., no significant difference between suicidal offenders and non-offenders).

The regions within the SBM source that differentiated suicide attempters from the two comparison groups overlapped to some extent with those identified in prior suicide studies. The posterior cingulate, precuneus, and cuneus comprised a prominent part of Source 29. While some studies have found the PCC to be associated with suicidal behavior (K. van Heeringen et al. 2014; Silvers et al. 2016), other studies have not. Because these regions are nodes in the default network (Raichle et al. 2001; Buckner et al. 2008; Harrison et al. 2008), it has been suggested that they represent mind-wandering and a reduced ability to inhibit intrusive thoughts in the context of suicidal ideation (Minzenberg et al. 2015). Consistent with this suggestion, a recent study found that precuneus and cuneus activation were positively correlated with emotion regulation success (the ability to distance oneself from aversive memories) in suicide attempters but not non-attempters (Silvers et al. 2016). However, the present study is the first to report an association between suicidal behavior and precuneus GM. Whether the findings reflect an interaction between suicidality, brain structure, and the unique characteristics of the forensic sample (see below) remains to be determined.

Also in line with the proposed association between Source 29 regions and reduced ability to regulate emotional responses is the inclusion of several prefrontal regions, primarily corresponding to Brodmann Areas 6, 8 and 10. The involvement of these regions, particularly dorsal and lateral subregions, in the regulation of emotional responses is well established (Phillips et al. 2008; Ochsner et al. 2012). Ding et al. (2015) reported reduced dorsal prefrontal volume, and associations with specific features of suicidal behavior (lethality and number of attempts) in a dorsal prefrontal region that included BA8. Additionally, an fMRI study in a small female sample reported reduced prefrontal activity, in a region that closely overlapped the BA10 region contained within Source 29, when recalling autobiographical details of a recent suicide attempt (Reisch et al. 2010). The association between other specific prefrontal regions included in Source 29 (e.g., BA 6) and suicidal behavior requires further investigation.

Source 29 also included the left amygdala. Along with prefrontal cortex, the amygdala is one of the most consistently implicated regions in emotion regulation. It is a common site of PFC modulation by during emotion regulation tasks such as cognitive reappraisal (Wager et al. 2008; Ochsner et al. 2012). It has also been linked to rumination in the context of cognitive reappraisal (i.e., greater amygdala activation during appraisal in those with higher rumination tendencies). However, amygdala volume has not typically been associated with suicidal behavior in prior studies. Like the PCC/precuneus, along with other regions included in Source 29 but not associated with suicidal behavior in prior studies, it is possible that the involvement of the amygdala in suicidal behavior is more relevant for forensic populations. It is also possible that the involvement of these regions is driven primarily by their interrelationship with the other Source 29 regions. This emphasizes the importance of multivariate investigations of brain structure (and function) in suicidal behavior.

Source 29 also included several peaks within the inferior parietal cortex and posterior STG. Prior studies have reported reduced volume in this region in suicide attempters relative to non-attempters (Monkul et al. 2007; Aguilar et al. 2008; Giakoumatos et al. 2013). Associations between pSTG and suicidal behavior may represent altered social perception -

inferred perceptions of oneself by others which lead to negative affect (Giakoumatos et al. 2013).

In contrast to prior studies of suicidal behavior in non-offender samples (Ding et al., 2015; Johnston et al., 2017, Duarte et al., 2017) neither the orbitofrontal cortex (OFC) nor anterior cingulate (ACC) were included in Source 29, nor were any significant differences between suicide attempters and non-attempters in these regions found in the VBM analysis. This may suggest that the neural substrates of suicidal behavior differ depending on the population (community, offender, psychiatric). It may also be related to the extent to which non-imaging risk factors for suicide apply to a particular group. For example, the OFC is strongly implicated in drug abuse (Volkow and Fowler 2000; London et al. 2000; Schoenbaum et al. 2006), which is a risk factor for suicidal behavior (Arsenault-Lapierre et al. 2004; Blaauw et al. 2005). Nearly all participants in this study had a drug use disorder, which precluded examining its relation to suicidal behavior. This may explain why we did not find group differences in OFC.

We did not observe significant associations between non-imaging risk factors and suicidal behavior, although the effects were in the expected direction (e.g., higher depression and early trauma rates). This may be due to the small sample size, or potential sources of heterogeneity in the prison sample that were not accounted for in this study. The findings may also indicate that imaging measures, particularly using multivariate analysis techniques such as SBM, are more sensitive indicators of risk for suicidal behavior.

The results highlight the overall utility of multivariate (i.e., ICA) approaches to neuroimaging data analysis. For example, in the SBM analysis, artifact components (e.g. motion, physiological) were extracted prior to subsequent analysis. There are no such corrections in VBM analysis. Thus, potentially greater noise in the VBM data may have obscured relevant results or made them less robust. As shown in the results, while both VBM and SBM analyses implicated the PCC in suicidal behavior, only the SBM results showed group differences between suicidal offenders and both non-suicidal offenders and non-offenders in this region.

There are some limitations to this study. First, our assessment of suicidal behavior was retrospective. While studies have shown that that suicide risk is measurable up to 37 years after the initial attempt (Angst et al. 2005; Bradvik et al. 2008; Dahlgren 1977; Suominen et al. 2004), prospective studies in which neuroimaging measures are recorded at baseline (prior to suicidal behavior) will provide a more stringent test of their applicability as risk variables. Second, although having a history of suicide attempts is a strong indicator of future suicide, many attempters will not go on to complete. Prospective studies are needed to determine whether the current results extend to suicide completion. Third, we did not include a comparison group of non-offenders with past suicide attempts. As such, the question of whether the current results are generalizable to non-offender populations cannot be addressed. Criminal offenders may have characteristics related to suicidal behavior that distinguish them from suicidal non-offenders, such as: 1) higher risk for lethal suicide attempts due to capability, prior exposure/desensitization, and access to lethal means, 2) higher prevalence of other risk factors for suicide including substance abuse, impulsivity,

and aggression, 3) greater vulnerability to feelings of isolation and perceived burdensomeness to others (e.g., family) related to their incarceration. Also, we did not examine specific characteristics of suicidal behavior such as lethality, which was associated with reduced dPFC volume in Ding et al. (2015). Nor was information regarding the number of attempts per subject available. Lastly, the sample size was relatively small. Replication in larger samples will be useful to support the current study results and may provide additional insights.

The current results do not demonstrate reduced connectivity between brain regions in suicide attempters, which are best studied using functional and diffusion methods. Rather, the current results indicate reduced gray matter volume in a source that has shared morphological features. Although replication is needed, the current results are of clinical interest in that they identify a potential biomarker of suicide risk in a high-risk population that may be useful in the assessment of suicide risk and/or represent a target for treatment and risk management.

Acknowledgments

Funding This work was supported by grants from the National Institutes of Health (P20GM103472; R01DA026505; R01MH070539).

References

- Aguilar EJ, García-Martí G, Martí-Bonmatí L, Lull JJ, Moratal D, Escartí MJ, et al. (2008). Left orbitofrontal and superior temporal gyrus structural changes associated to suicidal behavior in patients with schizophrenia. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 32(7), 1673–1676. [PubMed: 18657587]
- Angst J, Angst F, Gerber-Werder R, & Gamma A (2005). Suicide in 406 mood-disorder patients with and without long-term medication: a 40 to 44 years' follow-up. *Archives of Suicide Research*, 9(3), 279–300. [PubMed: 16020171]
- Arsenault-Lapierre G, Kim C, & Turecki G (2004). Psychiatric diagnoses in 3275 suicides: a meta-analysis. *BMC Psychiatry*, 4(1), 37. [PubMed: 15527502]
- Ashburner J, & Friston KJ (2005). Unified segmentation. *Neuroimage*, 26(3), 839–851. [PubMed: 15955494]
- Benedetti F, Radaelli D, Poletti S, Locatelli C, Falini A, Colombo C, et al. (2011). Opposite effects of suicidality and lithium on gray matter volumes in bipolar depression. *Journal of Affective Disorders*, 135(1), 139–147. [PubMed: 21807414]
- Blaauw E, Kerkhof AJFM, & Hayes LM (2005). Demographic, criminal, and psychiatric factors related to inmate suicide. *Suicide and Life-Threatening Behavior*, 35(1), 63–75. [PubMed: 15843324]
- Brådvik L, Mattisson C, Bogren M, & Nettelbladt P (2008). Long-term suicide risk of depression in the Lundby cohort 1947–1997—severity and gender. *Acta Psychiatrica Scandinavica*, 117(3), 185–191. [PubMed: 18190676]
- Briere J, & Elliott DM (2003). Prevalence and psychological sequelae of self-reported childhood physical and sexual abuse in a general population sample of men and women. *Child Abuse and Neglect*, 27, 1205–1222. [PubMed: 14602100]
- Brown GK, Beck AT, Steer RA, & Grisham JR (2000). Risk factors for suicide in psychiatric outpatients: a 20-year prospective study. *Journal of Consulting and Clinical Psychology*, 68(3), 371. [PubMed: 10883553]
- Buckner RL, Andrews-Hanna JR, & Schacter DL (2008). The brain's default network. *Annals of the New York Academy of Sciences*, 1124(1), 1–38. [PubMed: 18400922]

- Dahlgren K (1977). Attempted suicides—35 years afterward. *Suicide and Life-Threatening Behavior*, 7(2), 75–79. [PubMed: 613505]
- Ding Y, Lawrence N, Olie E, Cyprien F, Le Bars E, Bonafe A, Phillips ML, Courtet P & Jollant F (2015). Prefrontal cortex markers of suicidal vulnerability in mood disorders: a model-based structural neuroimaging study with a translational perspective. *Translational Psychiatry*, 5(2), e516. [PubMed: 25710122]
- Douglas KS, Lilienfeld SO, Skeem JL, Poythress NG, Edens JF, & Patrick CJ (2008). Relation of antisocial and psychopathic traits to suicide-related behavior among offenders. *Law and Human Behavior*, 32(6), 511–525. [PubMed: 18080733]
- Duarte DG, Maila de Castro LN, Albuquerque MR, Turecki G, Ding Y, de Souza-Duran FL, Busatto G, & Correa H (2017). Structural brain abnormalities in patients with type I bipolar disorder and suicidal behavior. *Psychiatry Research: Neuroimaging*, 265, 9–17. [PubMed: 28494347]
- Dube SR, Anda RF, Felitti VJ, Chapman DP, Williamson DF, & Giles WH (2001). Childhood abuse, household dysfunction, and the risk of attempted suicide throughout the life span: findings from the Adverse Childhood Experiences Study. *JAMA*, 286(24), 3089–3096. [PubMed: 11754674]
- First MB, Spitzer RL, Gibbon M, & Williams JBW (1997). *Structured Clinical Interview for DSM-IV Axis I Disorders – Clinical Version (SCID-IV)*. Washington, D.C.: American Psychiatric Press.
- Giakoumatos CI, Tandon N, Shah J, Mathew IT, Brady RO, Clementz BA, et al. (2013). Are structural brain abnormalities associated with suicidal behavior in patients with psychotic disorders? *Journal of Psychiatric Research*, 47(10), 1389–1395. [PubMed: 23866739]
- Gunnell D, & Lewis G (2005). Studying suicide from the life course perspective: implications for prevention. *The British Journal of Psychiatry*, 187(3), 206–208. [PubMed: 16135856]
- Hare RD (2003). *The Hare Psychopathy Checklist-Revised*. Toronto: Multi-Health Systems.
- Harrison BJ, Pujol J, López-Solà M, Hernandez-Ribas R, Deus J, Ortiz H, et al. (2008). Consistency and functional specialization in the default mode brain network. *Proceedings of the National Academy of Sciences*, 105(28), 9781–9786.
- Hwang JP, Lee TW, Tsai SJ, Chen TJ, Yang CH, Lim JF, & Tsai CF (2010). Cortical and subcortical abnormalities in late-onset depression with history of suicide attempts investigated with MRI and voxel-based morphometry. *Journal of Geriatric Psychiatry and Neurology*, 23(3), 171–184. [PubMed: 20430976]
- Jenkins R, Bhugra D, Meltzer H, Singleton N, Bebbington P, Brugha T, et al. (2005). Psychiatric and social aspects of suicidal behaviour in prisons. *Psychological Medicine*, 35(2), 257–269. [PubMed: 15841683]
- Johnston JA, Wang F, Liu J, Blond BN, Wallace A, Liu J, Spencer L, Cox Lippard ET, Purves KL, Landeros-Weisenberger A, & Hermes E (2017). Multimodal neuroimaging of frontolimbic structure and function associated with suicide attempts in adolescents and young adults with bipolar disorder. *American Journal of Psychiatry*, 174(7), 667–675. [PubMed: 28135845]
- Jollant F, Lawrence NS, Giampietro V, Brammer MJ, Fullana MA, Drapier D, et al. (2008). Orbitofrontal cortex response to angry faces in men with histories of suicide attempts. *American Journal of Psychiatry*.
- Kašpárek T, Mareš R, Schwarz D, Píškryl R, Vaníček J, Mikl M, et al. (2010). Source-based morphometry of gray matter volume in men with first-episode schizophrenia. *Human Brain Mapping*, 31(2), 300–310.
- Li YO, Adah T, & Calhoun VD (2007). Estimating the number of independent components for functional magnetic resonance imaging data. *Human Brain Mapping*, 28(11), 1251–1266. [PubMed: 17274023]
- London ED, Ernst M, Grant S, Bonson K, & Weinstein A (2000). Orbitofrontal Cortex and Human Drug Abuse: Functional Imaging. *Cerebral Cortex*, 10(3), 334–342. [PubMed: 10731228]
- Minzenberg MJ, Lesh TA, Niendam TA, Yoon JH, Cheng Y, Rhoades RN, et al. (2015). Control-related frontal-striatal function is associated with past suicidal ideation and behavior in patients with recent-onset psychotic major mood disorders. *Journal of affective disorders*, 188, 202–209. [PubMed: 26363618]

- Monkul E, Hatch JP, Nicoletti MA, Spence S, Brambilla P, Lacerda A. L. T. d., et al. (2007). Fronto- limbic brain structures in suicidal and non-suicidal female patients with major depressive disorder. *Molecular Psychiatry*, 12(4), 360–366. [PubMed: 17389903]
- Nock MK, & Kessler RC (2006). Prevalence of and risk factors for suicide attempts versus suicide gestures: Analysis of the National Comorbidity Survey. *Journal of Abnormal Psychology*, 115(3), 616–623. [PubMed: 16866602]
- Ochsner KN, Silvers JA, & Buhle JT (2012). Functional imaging studies of emotion regulation: a synthetic review and evolving model of the cognitive control of emotion. *Annals of the New York Academy of Sciences*, 7257(1), E1–E24.
- Pan L, Hassel S, Segreti A, Nau S, Brent D, & Phillips M (2013). Differential patterns of activity and functional connectivity in emotion processing neural circuitry to angry and happy faces in adolescents with and without suicide attempt. *Psychological medicine*, 43(10), 2129–2142. [PubMed: 23298821]
- Patton JEL, Stanford MS, & Barratt ES (1995). Factor structure of the barratt impulsiveness scale. *Journal of Clinical Psychology*, 51(6), 768–774. [PubMed: 8778124]
- Phillips ML, Ladouceur CD, & Drevets WC (2008). A neural model of voluntary and automatic emotion regulation: implications for understanding the pathophysiology and neurodevelopment of bipolar disorder. *Molecular Psychiatry*, 75(9), 833–857.
- Posner K, Brown GK, Stanley B, Brent DA, Yershova KV, Oquendo MA, et al. (2011). The Columbia–Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. *American Journal of Psychiatry*.
- Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, & Shulman GL (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences*, 98(2), 676–682.
- Reisch T, Seifritz E, Esposito F, Wiest R, Valach L, & Michel K (2010). An fMRI study on mental pain and suicidal behavior. *Journal of affective disorders*, 126(1-2), 321–325. [PubMed: 20434779]
- Rentería ME, Schmaal L, Hibar DP, Couvy-Duchesne B, Strike LT, Mills NT, de Zubicaray GL, McMahon KL, Medland SE, Gillespie NA, & Hatton SN (2017). Subcortical brain structure and suicidal behaviour in major depressive disorder: a meta-analysis from the ENIGMA-MDD working group. *Translational Psychiatry*, 7(5), e1116. [PubMed: 28463239]
- Ryan JJ, Lopez SJ, & Werth TR (1999). Development and preliminary validation of a Satz-Mogel short form of the Wais-III in a sample of persons with substance abuse disorders. *International Journal of Neuroscience*, 98, 131–140. [PubMed: 10395365]
- Scheuerecker J, Meisenzahl EM, Koutsouleris N, Linn J, Wiesmann M, Bruckmann H, et al. (2010). Orbitofrontal volume reductions during emotion recognition in patients with major depression. *Journal of psychiatry & neuroscience: JPN*, 35(5), 311. [PubMed: 20569645]
- Schoenbaum G, Roesch MR, & Stalnaker TA (2006). Orbitofrontal cortex, decision-making and drug addiction. *Trends in Neurosciences*, 29(2), 116–124. [PubMed: 16406092]
- Silvers JA, Hubbard AD, Chaudhury S, Biggs E, Shu J, Grunebaum MF, et al. (2016). Suicide attempters with Borderline Personality Disorder show differential orbitofrontal and parietal recruitment when reflecting on aversive memories. *Journal of Psychiatric Research*, 81, 71–78. [PubMed: 27392071]
- Suominen K, Isometsä E, Suokas J, Haukka J, Achte K, & Lönnqvist J (2004). Completed suicide after a suicide attempt: a 37-year follow-up study. *American Journal of Psychiatry*, 161(3), 562–563. [PubMed: 14992984]
- Swann AC, Dougherty DM, Pazzaglia PJ, Pham M, Steinberg JL, & Moeller FG (2005). Increased impulsivity associated with severity of suicide attempt history in patients with bipolar disorder. *American Journal of Psychiatry*, 162(9), 1680–1687. [PubMed: 16135628]
- Swanson JW, Swartz MS, Van Dorn RA, Elbogen EB, Wagner HR, Rosenheck RA, et al. (2006). A national study of violent behavior in persons with schizophrenia. *Archives of General Psychiatry*, 63(5), 490–499. [PubMed: 16651506]
- Swogger MT, You S, Cashman-Brown S, & Conner KR (2011). Childhood physical abuse, aggression, and suicide attempts among criminal offenders. *Psychiatry Research*, 185(3), 363–367. [PubMed: 20724000]

- van Heeringen K, Bijttebier S, Desmyter S, Vervaet M, & Baeken C (2014). Is there a neuroanatomical basis of the vulnerability to suicidal behavior? A coordinate-based meta-analysis of structural and functional MRI studies. *Frontiers in Human Neuroscience*, 8, 824. [PubMed: 25374525]
- van Heeringen K, & Mann JJ (2014). The neurobiology of suicide. *The Lancet Psychiatry*, 1(1), 63–72. [PubMed: 26360403]
- Volkow ND, & Fowler JS (2000). Addiction, a disease of compulsion and drive: Involvement of the orbitofrontal cortex. *Cerebral Cortex*, 10(3), 318–325. [PubMed: 10731226]
- Wager TD, Davidson ML, Hughes BL, Lindquist MA, & Ochsner KN (2008). Prefrontal-subcortical pathways mediating successful emotion regulation. *Neuron*, 59(6), 1037–1050. [PubMed: 18817740]
- Wagner G, Koch K, Schachtzabel C, Schultz CC, Sauer H, & Schlösser RG (2011). Structural brain alterations in patients with major depressive disorder and high risk for suicide: evidence for a distinct neurobiological entity? *Neuroimage*, 54(2), 1607–1614 [PubMed: 20832482]
- Wagner G, Koch K, Schachtzabel C, Peikert G, Sauer H, & Schlösser R (2008). Enhanced rostral anterior cingulate cortex activation during cognitive control is related to orbitofrontal volume reduction in unipolar depression. *Journal of affective disorders*, 107, S76–S77.
- Wechsler D (1997). Wechsler Adult Intelligence Scale. New York: Psychological Corporation.
- Wolf RC, Huber M, Lepping P, Sambataro F, Depping MS, Karner M, et al. (2014). Source-based morphometry reveals distinct patterns of aberrant brain volume in delusional infestation. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 48, 112–116. [PubMed: 24120443]
- Xu L, Groth KM, Pearlson G, Schretlen DJ, & Calhoun VD (2009). Source-based morphometry: The use of independent component analysis to identify gray matter differences with application to schizophrenia. *Human Brain Mapping*, 30(3), 711–724. [PubMed: 18266214]
- Zalsman G, Hawton K, Wasserman D, van Heeringen K, Arensman E, Sarchiapone M, et al. Suicide prevention strategies revisited: 10-year systematic review. *Lancet Psychiatry* (2016)3:646–59. [PubMed: 27289303]

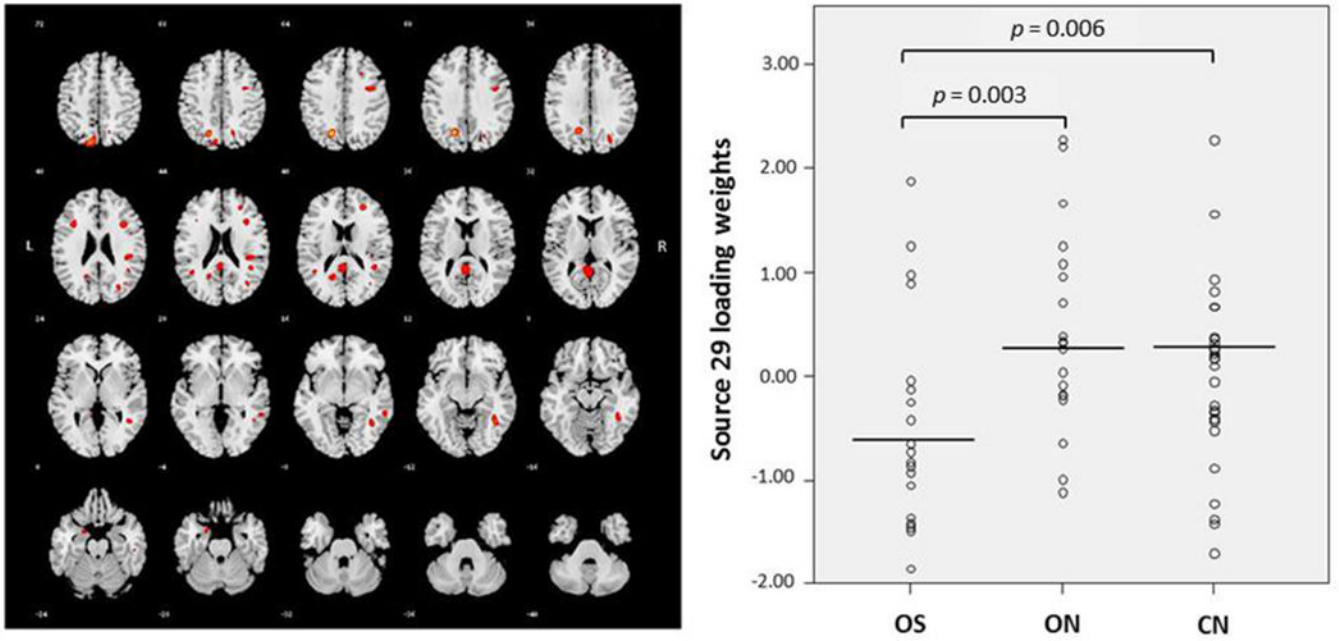


Fig. 1. Source 29 regions (left) and comparison of loading weights across group (right; p-values corrected for multiple comparisons). *OS*: Offenders with past suicide attempts, *ON*: Offenders with no past attempts, *CN*: Community Non-offenders

Table 1.

Demographic and clinical characteristics, and total brain volume, across study groups.

	Community Non-offender (n=26)	Offender No Suicide Attempt (n=19)	Offender Suicide Attempt (n=19)	Post Hoc		
	<i>M(SD)</i>	<i>M(SD)</i>	<i>M(SD)</i>	<i>F/t</i>	<i>p</i>	
Age	31.3 (9.90)	35.9 (7.69)	36.6 (7.99)	2.63	0.08	---
IQ Estimate	119.3 (13.32)	101.0 (12.62)	101.7 (16.18)	12.85	<.001	CN>ON/OS
PCL-R	***	20.8 (5.71)	20.5 (9.31)	0.12	0.90	---
BIS	***	70.39 (15.42)	75.21 (10.73)	1.12	0.27	---
TBV	1240.36	1209.37	1174.99	2.71	0.08	---
	%	%	%	χ^2	<i>p</i>	
Race (CA:AA:OT)	56:11:33	58:10.5:31.5	58:10.5:31.5	0.04	1.00	---
Handedness (R:L:B)	89:4:7	74:5:21	95:0:5	4.13	0.39	---
Depression	0	11	32	10.38	<.01	CN<ON/OS
AUD	0	74	68	32.92	<.001	CN<ON/OS
DUD	0	79	100	52.24	<.001	CN<ON<OS
Early Abuse	***	32	63	3.80	0.05	OS>ON
Serious Aggression	***	74	63	0.49	0.48	---
ASPD	0	74	63	31.23	<.001	CN<ON/OS

IQ: Intelligence quotient estimate from the vocabulary and matrix reasoning subtests of the WAIS. CA: Caucasian, AA: African American, OT: Other. R: Right, L: Left, B: Both (no dominant hand). PCL-R = Psychopathy Checklist-Revised score. TBV = Total Brain Volume. BIS = Barratt Impulsivity Scale Score. AUD = Alcohol Use Disorder. DUD = Drug Use Disorder. ASPD = Antisocial Personality Disorder.

*** Community non-offenders completed an abbreviated protocol which did not include assessment of these variables, or the variable was not relevant to the population (e.g., serious aggression).

Table 2.

Logistic regression analysis evaluating suicide attempt history (yes/no) in offenders based on clinical variables.

Risk Variable	β	SE(β)	p value	OR (95% CI)
Depression	1.37	0.90	0.13	3.92 (0.68 – 22.71)
Alcohol Use Disorder	0.26	0.72	0.72	0.77 (0.19 – 3.16)
Early Abuse	1.31	0.69	0.06	3.71 (0.97 - 14.23)
Impulsivity	0.39	0.35	0.27	1.47 (0.74 - 2.94)
Aggression	-0.49	0.71	0.49	0.61 (0.15 - 2.44)

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 3.

List of MNI coordinates and regions comprising Component 29.

Region	BA	MNI (x,y,z)
Precuneus	7	(-18, -61, 39; 12, -73, 51; -7, -67, 56)/(18, -60, 44)
Posterior Cingulate	29, 30	(-1, -44, 15)/(4, -51, 9)
Inferior Parietal Lobule	40	(45, -28, 22)
Precentral Gyrus	6, 9	(37, 3, 37)
Insula	13	(42, -30, 19; 42, -43, 21)
Cingulate Gyrus	31	(-13, -55, 29)
Middle Temporal Gyrus	19/39, 37, 21	(-39, -63, 21)/(46, -52, 3; 59, -42, -3)
Fusiform Gyrus	37	(42, -46, -12)
Superior Temporal Gyrus	39	(-42, -49, 20)/(45, -44, 19; 45, -45, 23; 46, -48, 26)
Superior Frontal Gyrus	6	(-16, -11, 64; -13, -8, 64; -13, -11, 61)
Middle Frontal Gyrus	10	(31, 46, 13; 28, 49, 16; 24, 49, -2)
Middle Frontal Gyrus	6,8	(45, 3, 33); (34, 3, 40)
Cerebellum	---	(-28, -75, -42)/(21, -59, -42; 27, -62, -40)
Amygdala	---	(-19, 0, -21)
Parahippocampal Gyrus	30	(-10, -46, 4)
Superior Parietal Lobule	7	(-21, -63, 45)
Superior Occipital Gyrus	39	(34, -74, 27)
Cuneus	17, 19	(-12, -74, 9)/(12, -71, 8; 28, -74, 30)
Inferior Temporal Gyrus	20	(53, -27, -19)
Inferior Temporal Gyrus	38	(-52, -2, -33)