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Latent-Variable Modeling of Brain Gray-Matter Volume and Psychopathy in Incarcerated Offenders

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CITATION

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Advanced statistical modeling has become a prominent feature in psychological science and can be a useful approach for representing the neural architecture linked to psychopathy. Psychopathy, a disorder characterized by dysfunction in interpersonal-affective and impulsive-antisocial domains, is associated with widespread neural abnormalities. Several imaging studies suggest that underlying structural deficits in paralimbic regions are associated with psychopathy. Although these studies are useful, they make assumptions about the organization of the brain and its relevance to individuals displaying psychopathic features. Capitalizing on statistical modeling, in the present study (N = 254), we used latent-variable methods to examine the structure of gray-matter volume in male offenders, and assessed the latent relations between psychopathy and gray-matter factors reflecting paralimbic and nonparalimbic regions. Results revealed good fit for a 4-factor gray-matter paralimbic model and these first-order factors were accounted for by a superordinate paralimbic “system” factor. Moreover, a superordinate psychopathy factor significantly predicted the paralimbic, but not the nonparalimbic factor. The latent-variable paralimbic model, specifically linked with psychopathy, goes beyond understanding single brain regions within the system and provides evidence for psychopathy-related gray-matter volume reductions in the paralimbic system as a whole.

General Scientific Summary
In the present study, we applied statistical methods to mathematically model gray-matter volume and examine underlying structural deficits in psychopathy. Results indicated that the latent brain factors are in accordance with standard thinking regarding basic neuroanatomy. Moreover, psychopathy was negatively related to paralimbic regions and was differentially predictive of the system structure compared with brain areas outside of the paralimbic system.

Keywords: psychopathy, gray matter, offenders, structural equation modeling

Increasingly, understanding the nature of constructs through modeling has become a prominent feature in psychological science (Hoyle, 2012). Latent-variable approaches have been used to mathematically model the structure of normal-range personality (Marsh et al., 2010), intelligence (Decker, Englund, & Roberts, 2014), general psychopathology (Caspí et al., 2013), and psychopathic traits (Neumann, Hare, & Pardini, 2015). In addition, latent-variable models have been used to understand brain data in schizophrenia from magnetic resonance imaging (MRI; Tien et al., 1996), neuronal networks from functional MRI (fMRI; Lahey et al., 2012), intracerebral volumetric relationships in twins (Schmitt et al., 2010), and cortical connections in basic neuroscience research (McIntosh & Gonzalez-Lima, 1994). The use of statistical modeling to mathematically represent phenomena and then test assumptions about the relationship between latent-brain and behavior variables provides a sophisticated approach to further elu-
Psychopathy, a personality disorder involving chronic antisocial behavior along with interpersonal and emotional disturbances, has been associated with widespread disruptions in brain morphology. Drawing on early functional data and clinical studies of behavioral changes following lesions (e.g., orbital frontal patients), Kiehl (2006) postulated that disturbances in the limbic/paralimbic system as a whole contribute to psychopathy-related problems engaging in adaptive behavior. Consistent with Kiehl’s (2006) paralimbic hypothesis, subsequent structural imaging studies of psychopathic individuals found thinner cortex in multiple areas, including the left insula, left dorsal anterior cingulate cortex (ACC), the left and right precentral gyrus, the left and right temporal poles, the right inferior frontal gyrus (Ly et al., 2012) and the frontal and temporal lobes (Müller et al., 2003), the bilateral parahippocampal and hippocampal regions and the amygdala, the bilateral temporal pole, posterior cingulate cortex, as well as, the orbitofrontal cortex (OFC; Ermer, Cope, Nyalakanti, Calhoun, & Kiehl, 2012). Despite evidence for paralimbic dysfunction in psychopathy, studies have shown that not all limbic/paralimbic regions reach significance in relation to psychopathy, which limits support for a system-wide model.

Previous structural imaging research, although aiming for whole-brain analysis, often still involves examination of individual brain regions, and extrapolation regarding the multiplicity of regional disruptions to a system-wide disruption. In addition, investigators must assume that the pattern of regional findings map onto existing knowledge about the organization of the neural system and their relevance for individuals expressing psychopathy. These critical issues should be addressed in further research to comprehensively test the applicability of the paralimbic model for psychopathy. One approach to test system-based assumptions uses statistical modeling. As suggested by McIntosh and Protzer (2012), “If it is the case that brain function results from the action of distributed networks, then analytic approaches tuned to such dynamics would best capture these actions. One method that has proven useful . . . is structural equation modeling (SEM)” (p. 636).

The goal of the current study was to use latent-variable methods to examine the structure of the paralimbic gray-matter volume in offenders, and assess the relationship between psychopathy and gray-matter factors reflecting paralimbic and nonparalimbic regions. The advantages of latent-variable modeling are considerable, such as, its formal accounting of measurement error (i.e., noise) separately from common variance (i.e., signal) to precisely gauge associations between phenomena (e.g., Baskin-Sommers et al., 2015), as well as the delineation of the dimensionality of a given assessment (Neumann et al., 2015). Moreover, SEM is ideal for development of latent-variable models that mathematically represent biological and psychological phenomena in terms of rigorous testable models and precisely estimate the degree of association between brain and behavior (Bollen, 2002; Smith, McCarthy, & Zapolski, 2009). With regard to psychopathy, an accurate estimate of the link between psychopathy and gray-matter volume would be helpful, because current estimates based on a manifest-variable (i.e., a variable that can be directly measured) approaches vary widely (–.11 to –.79; Yang & Raine, 2009). Mathematical modeling of the entire paralimbic system involved in psychopathy may provide a comprehensive structural representation, with associated model parameters, to characterize the brain–behavior relationships in psychopathy.

Method

Participants

Study participants were 254 male inmates from medium-maximum-security correctional facilities in New Mexico who were enrolled in the South West Advanced Neuroimaging Cohort, Adult (SWANC-A) sample (see Ermer et al., 2012 for a different type of analysis with the same data). Individuals were excluded if they read at a fourth-grade level or lower on a standardized measure of reading (i.e., the Wide Range Achievement Test–III; Wilkinson, 1993), scored below 70 on a brief measure of IQ (Wechsler Adult Intelligence Scale–III; Wechsler, 1997), had diagnoses of schizophrenia, bipolar disorder, or psychosis, not otherwise specified (Structured Clinical Interview for Axis-II DSM Personality Disorders; First, Gibbon, Spitzer, Williams, & Benjamin 1997), or had a history of medical problems (e.g., uncorrectable auditory or visual deficits; head injury with loss of consciousness greater than 30 min) that might have impacted their comprehension of the materials. All inmates were assessed using the Hare Psychopathy Checklist–Revised (PCL-R; Hare, 2003). The descriptive statistics for the PCL-R were consistent with previous reports ($M = 20.83, SD = 6.77, range = 3–36$). Of the 254 cases, 28 (11%) were at or above cut-off for psychopathy. Using approximately 10% of the interviews, interrater reliability (i.e., intraclass correlation coefficient) was .96 for total scores and $\alpha$ was good for the total sample (.81). The University of New Mexico Health Sciences Center Institutional Review Board approved this research, and inmates volunteered to participate after providing written informed consent. Participants were paid for their participation at the rate of $1/hr, comparable with institutional wages for labor.

Covariates

Several covariates were used to adjust for individual variation in extraneous factors that have been known to impact antisocial behavior and brain development. First, age ($M = 28.43, SD = 9.09$) was used as a covariate because antisocial behavior and the effects of psychopathy have been found to change with advancing age (Steffensmeier, Allan, Harer, & Streifel, 1989). Second, total years of regular substance use (three or more times per week) was included as a covariate ($M = 15.85, SD = 12.11$). Third, estimated IQ was included as a covariate ($M = 96.28, SD = 13.78$). Finally, in supplemental model analyses, brain volume (white matter + gray matter) was included as a covariate since volumetric analyses regularly control for individual variation in brain size. Brain volume was not significantly correlated with PCL-R scores (Hare, 2003), though was generally modestly correlated with age ($-.33$),
IQ (.21), substance use (−.08), and the brain-region variables (−.17 to .31) used in model analyses (ps < .001). The pattern of results was substantively unchanged when brain volume was included in the analyses.

MRI Acquisition

High-resolution T1-weighted structural MRI scans were acquired on the Mind Research Network’s Siemens 1.5T Avanto mobile scanner stationed at the correctional facility using a magnetization-prepared rapid gradient-echo (MPRAGE) pulse sequence (repetition time = 2,530 ms, echo times = 1.64 ms, 3.50 ms, 5.36 ms, 7.22 ms, inversion time = 1,100 ms, flip angle = 7°, slice thickness = 1.3 mm, matrix size = 2562) that yielded 128 sagittal slices with an in-plane resolution of 1 mm2. Data were preprocessed and analyzed using Statistical Parametric Mapping software (SPM5; Wellcome Department of Cognitive Neurology, London, UK; 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. Images were then spatially normalized to the T1 Montreal Neurological Institute (MNI) template, resampled to 2 mm3, segmented into gray matter, white matter, and cerebrospinal fluid, and modulated to preserve total volume (Ashburner & Friston, 2000, 2005). Voxels with a matter value of >.15 were excluded to remove possible edge effects between gray and white matter. Segmented images were smoothed with a 10-mm full-width at half-maximum Gaussian kernel.

For the present study, voxel-based morphometric (VBM) limbic/paralimbic variables were used for latent-variable model analyses. The VBM variables reflected the following regions: ACC, posterior cingulate cortex (PCC), left and right parahippocampal gyrus, left and right amygdala, left and right hippocampus, left and right temporal pole, left and right lateral OFC, left and right insula, and medial OFC (Kiehl, 2006). Also, two nonparalimbic regions involving the primary visual cortex, Broadman’s Area (BA) 17 and the motor cortex (BA 4) were included. Based on earlier theory, the choice to include the motor and visual cortical gray-matter regions as indicators of a latent nonparalimbic variable was ideal, given that these regions lie far outside of the paralimbic system. Ultimately, the inclusion of these regions provides a test of the differential predictive validity of psychopathy on the paralimbic system versus nonparalimbic areas of the brain. The nonparalimbic VBM variables were significantly correlated, r = .40, p < .001, and could be represented by a single latent variable: comparative fit index (CFI) = 1.0, root-mean-square error of approximation (RMSEA) = .00.

Analytic Strategy

First, the structure of the VBM variables was examined by conducting an exploratory factor analysis (EFA) using Mplus (Muthén & Muthén, 1998), which provides model-fit indices to help determine a viable factor solution. The EFA that was deemed the best solution was then subjected to a confirmatory factor analysis (CFA) by specifying the VBM variables to load only on their respective factor. The CFA-VBM model provided a rigorous test of the VBM-to-factor relations (i.e., the measurement model). In addition, the applicability of whether the first-order VBM factors could be loaded onto a superordinate paralimbic factor, thereby representing a broad paralimbic system factor, was tested. For these models, VBM variables were treated as continuous and maximum likelihood (ML) was used for parameter estimation.

Second, a CFA was conducted that included the PCL-R items (Hare, 2003) along with the VBM variables to gauge overall model fit at the measurement level and obtain precise estimates of how the VBM factors were correlated with PCL-R first-order factors. The PCL/VBM CFA also allowed us to check that the PCL-R factors were uniformly associated with the VBM factors before using a superordinate psychopathy factor to predict a superordinate VBM factor. The PCL-R item-to-factor specifications were modeled as in previous research (Neumann et al., 2015). The PCL-R items were set to load onto their respective factors: Interpersonal (Items 1, 2, 4, 5), Affective (Items 6, 7, 8, 16), Lifestyle (Items 3, 9, 13, 14, 15), and Antisocial (Items 10, 12, 18, 19, 20).

In a subsequent SEM analysis, the PCL-R first-order factors were set to load onto a single superordinate (second-order) factor, which has been shown to account for the variance in the first-order factors (Neumann, Hare, et al., 2007), the superordinate psychopathy factor set to predict the superordinate paralimbic factor, and the nonparalimbic factor. For these models, given the ordinal nature of the PCL-R items, the standard Mplus robust weighted least squares (WLSMV) estimation was used (Neumann, Kosson, & Salekin, 2007). In the SEM, age, substance use, and IQ were used as covariates.

For all analyses, as recommended by Hu and Bentler (1999), a two-index strategy was used to assess model fit: the incremental CFI and an absolute fit index, the RMSEA. Generally, CFI at or above .90 and RMSEA at or below .08 are considered acceptable model fit (Hoyle, 1995). Instead of relying on more stringent fit indices, traditional fit criteria (CFI ≥ .90, RMSEA ≤ .08) were used, given that as model complexity increases, so does the difficulty of achieving conventional levels of model fit (Marsh, Hau, & Wen, 2004). These standard fit criteria were used to avoid falsely rejecting viable latent-variable models. For the EFAs conducted with VBM data, the Bayesian information criterion (BIC) was used, which is available with ML estimation. Increasingly smaller values of BIC correspond to better fitting models. When comparing two models any BIC difference larger than 10 provides support for the model with the smaller BIC value (Raftery, 1995). Also, guidelines laid out by Cheung and Rensvold (2002) were used to assess statistical differences in model fit. If the incremental change in the comparative fit index (ΔCFI) between a superordinate model and a nested, more constrained, model is ≤.01, then it is reasonable to hold that the two models within the comparison do not differ statistically in terms of fit. Based on a simulation study, Cheung and Rensvold recommended that ΔCFI is more appropriate than the traditional way of assessing differences in the $\chi^2$ fit statistic between nested models.

Results

Exploratory Factor Analysis (EFA)

As shown in Table 1, a four-factor solution produced significantly lower BIC values than the solutions with one, two, or three factors. Moreover, there was less than a 10-point or more change in BIC value between the four- and five-factor EFA solutions, and...
there was no meaningful change in CFI between these two solutions. The four-factor solution was associated with excellent fit (CFI = 1.0, RMSEA = .01), and resulted in theoretically meaningful factors.

Table 2 displays the (oblique geomin-rotated) factor loadings for the four-factor VBM-EFA solution. The first factor to emerge was a broad VBM factor (referred to as medial orbital frontal/cingulate) that included the ACC, medial OFC, left and right insula, and PCC. The second factor to emerge was another broad VBM factor (orbital frontal/temporal pole) that included the left and right lateral OFC, as well as the left and right temporal pole. The third factor (left medial temporal) included the left parahippocampus, hippocampus, and amygdala VBM variables, and the fourth factor (right medial temporal) involved the right parahippocampus, hippocampus, and amygdala VBM variables. All factor loadings were strong, with minimal cross-loadings, suggesting that coherent unidimensional VBM factors were obtained.

**Confirmatory Factor Analysis (CFA)**

To provide a stringent test of the EFA-generated VBM factor solution, the VBM (manifest) variables were set to load only on the respective factor they were primarily associated with in the EFA solution (i.e., no cross-loadings). The CFA resulted in adequate model fit (CFI = .92, RMSEA = .09), though the absolute index was slightly higher than the recommended .08. All VBM variables loaded strongly on their respective factor (ps < .001), and the VBM factors were significantly intercorrelated (mean r = .42, range = .22–.88, ps < .001). Given this pattern of results, it was also noted that the four VBM factors could be set to load onto a second-order factor without substantive changes in model fit (CFI = .92), and thus found evidence for a superordinate paralimbic system factor.

Next, another CFA was run that included the PCL-R items (Hare, 2003) in conjunction with the VBM variables. This CFA provided an opportunity to examine the overall measurement model with both sets of variables included before moving on to the SEM analysis, and also to examine the latent-variable associations between the PCL-R and VBM first-order factors. The CFA model resulted in acceptable model fit (CFI = .91, RMSEA = .04), and all manifest variables loaded strongly and significantly onto their respective factors (ps < .01–.001). Similar to the VBM first-order factors, the intercorrelations among the PCL-R factors were significant (mean r = .58, range = .40–.70, ps < .001).

Table 3 displays the latent bivariate correlations between the PCL-R (Hare, 2003) and VBM first-order factors. Among the significant correlations, the PCL-R factors were uniformly associated with the VBM factors, indicating a consistent pattern of inverse associations across the PCL-R and VBM first-order factors. The latent-variable approach resulted in nine out of 16 correlations being at or near p = .05 (56%) versus 6 of 16 reaching significance (37%) in the manifest-variable approach. Because the former method accounts for measurement error, it provides arguably the more precise estimate of psychopathy–brain-region associations.

**Structural Equation Modeling (SEM)**

Finally, an SEM was run that had the superordinate PCL-R Psychopathy factor predict the superordinate Paralimbic and the Nonparalimbic factors (i.e., visual and motor cortex VBM variables). Figure 1 displays the standardized parameters and shows that that psychopathy factor had a moderate negative predictive effect on the paralimbic factor (r = .38, p < .001), but did not predict the Nonparalimbic factor (r = .03, ns). The SEM accounted for the observed data to a high degree of precision (RMSEA = .05), and
substantial variance in both the Paralimbic ($R^2 = .32$) and the Nonparalimbic ($R^2 = .34$) factors.

With respect to the covariates, consistent with previous imaging studies, age had a large negative predictive effect on both the Paralimbic ($- .56$, $p < .001$) and Nonparalimbic ($- .59$, $p < .001$) factors, whereas IQ had a more modest positive effect on these two factors ($.14$ and $.27$, respectively, $p s < .01$). Substance use had no effect on the VBM factors. In line with recent research, age was negatively associated with the Psychopathy factor, $r = -.26$, $p < .001$ (Olver & Wong, 2015). Also, substance use had a positive association with Psychopathy, $r = .16$, $p < .05$.

Table 3
Confirmatory Factor Analysis: Latent-Variable (and Manifest-Variable) Bivariate Correlations Between Gray Matter (VBM) and PCL-R Factors

<table>
<thead>
<tr>
<th>Psychopathy factors</th>
<th>Gray matter (VBM) latent factors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Medial orbital frontal/cingulate</td>
</tr>
<tr>
<td>Interpersonal</td>
<td>-.15* (-.11)</td>
</tr>
<tr>
<td>Affective</td>
<td>.07 (.02)</td>
</tr>
<tr>
<td>Lifestyle</td>
<td>-.01 (-.01)</td>
</tr>
<tr>
<td>Antisocial</td>
<td>.10 (.06)</td>
</tr>
</tbody>
</table>

Note. Latent variable correlations in bold; observed (manifest) variable correlations in parentheses ($rs \geq .15$, $ps < .05$–.01). * $p < .05$. ** $p < .01$. *** $p < .001$. ' $p = .06$.

Figure 1. LMTP = left medial temporal pole; RMTP = right medial temporal pole; OFC/TP = orbital frontal cortex/temporal pole; MOF/C = medial orbital frontal/cingulate. Dashed lines indicate nonsignificance (ns) and gray lines represent model covariates.
In addition, separate SEMs were conducted for each VBM factor to examine the predictive effects of the superordinate Psychopathy factor on each VBM factor, while also controlling for the effects of age, substance use, and IQ. The results for each SEM indicated adequate model fit to the data and that the model parameters accounted for the data (RMSEAs = .04–.06). For each SEM, the Psychopathy factor negatively predicted each VBM factor (structural prediction parameters ranged from −.20 to −.33).

**Discussion**

For the current study, we used an interdisciplinary approach (i.e., clinical psychology, latent-variable modeling, and brain imaging) to characterize psychopathy and one of its neurobiological correlates, gray-matter volume. The results highlight the use of SEM to represent the syndrome of psychopathy, the paralimbic system, and the precision of latent- versus manifest-variable approaches in modeling and gauging the association between psychopathy and brain structure. Four latent VBM brain factors (Medial OFC, Frontal/Temporal Pole, Left Medial Temporal Pole, and Right Medial Temporal Pole) showed meaningful covariation, at least in terms of gray-matter volume, and could be used to mathematically represent a broad, superordinate, Paralimbic system factor. These latent brain factors are in accordance with standard thinking regarding neuroanatomy, and thus may provide insight into the system of regions involved in paralimbic functioning. Finally, the superordinate Psychopathy factor significantly predicted the latent Paralimbic factor, but not the Nonparalimbic factor. It is noteworthy, though, that the Nonparalimbic factor had significantly correlated with the Paralimbic factor, and the covariates had similar effects on both VBM factors, while at the same time, the PCL-R Psychopathy factor only predicted the Paralimbic VBM factor. Thus, these results indicate that paralimbic gray-matter regions can be meaningfully modeled at the latent-variable level and are specifically linked to psychopathy, whereas systems (i.e., visual and motor) outside of the paralimbic system have no association with this syndrome. Overall, the VBM first-order factors may reflect broad structural markers of brain-behavior pathology in psychopathy that go beyond understanding of single brain regions, one at a time.

Statistical modeling has been used to better understand and represent normative personality traits, cognitive functions, and general psychopathology. The movement to integrate more mathematical modeling into research on psychological constructs provides an opportunity to rigorously test the putative factors making up human behavior, with fewer assumptions than traditional statistical analyses (i.e., single model-based tests of a whole system while accounting for measurement error vs. a series of error-prone manifest-variable analyses aimed at accounting for such systems). If research in abnormal psychology is to become a science focused on effect sizes of various psychological and biological phenomena, as opposed to null-hypothesis testing, then precision in mathematically representing psychobiological constructs and estimating parameters is vital. The study of psychopathy is one domain of abnormal psychology that highlights this tension between the statistical methods of hypothesis testing and effect sizes. For instance, manifest-variable effect sizes of −0.11, −0.15, and −0.79 have been reported for the association between brain structure and psychopathy (Yang & Raine, 2009). In contrast, the present SEM results indicate a predictive effect size of −0.38 between the superordinate Psychopathy and Paralimbic factors. This result may represent a best estimate because a comprehensive model of the paralimbic system was uncovered by data-driven analyses, and thus provided a sound target for prediction. The superordinate Paralimbic factor may offer the opportunity for smaller sample imaging studies to employ a broad paralimbic composite to associate with psychopathy. That is, the formation of a manifest-paralimbic (super) composite variable may provide a better means to document paralimbic system dysfunction in small-sample studies, rather than relying on separate and predetermined neural regions to estimate effects. Thus, the use of statistical modeling to gauge the association between neural architecture and psychopathy is an exciting avenue for future research.

Before concluding, limitations of the present study should be noted. First, the pattern of results may not generalize to nonclinical populations or to other assessment procedures for psychopathy. Second, the present sample was limited to males, and thus it is unclear whether gender or not plays a role in moderating the association between brain volume and psychopathy (but see Cope, Ermer, Nyalakanti, Calhoun, & Kiehl, 2014). Finally, the effect of age on gray-matter volume and psychopathy was substantial, though this is not unexpected and is consistent with other imaging studies. Despite the strong age effect, the findings showed that the psychopathy factor was still able to predict decreased paralimbic system gray-matter volume.

Psychopathy is a multifarious disorder, both in terms of the personality pathology and the neural abnormalities that are associated with it. Prior to the present study, no study attempted to represent the broad structural brain systems that are thought to be involved in the syndrome of psychopathy. Using a latent-variable approach, psychopathy appears specifically associated with decreased gray-matter volume in the extensive paralimbic system and not areas that lie outside of the paralimbic system. The presence of widespread problems in tissue health may indicate that the fundamental neural environment present in the paralimbic systems of psychopathic individuals is suboptimal.

**References**


