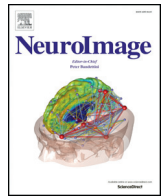




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## Q1 Machine learning of structural magnetic resonance imaging predicts 2 psychopathic traits in adolescent offenders

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### 1 1 A B S T R A C T

Classification models are becoming useful tools for finding patterns in neuroimaging data sets that are not observable to the naked eye. Many of these models are applied to discriminating clinical groups such as schizophrenic patients from healthy controls or from patients with bipolar disorder. A more nuanced model might be to discriminate between levels of personality traits. Here, as a proof of concept, we take an initial step toward developing prediction models to differentiate individuals based on a personality disorder: psychopathy. We included three groups of adolescent participants: incarcerated youth with elevated psychopathic traits (i.e., callous and unemotional traits and conduct disordered traits;  $n = 71$ ), incarcerated youth with low psychopathic traits ( $n = 72$ ), and non-incarcerated youth as healthy controls ( $n = 21$ ). Support vector machine (SVM) learning models were developed to separate these groups using an out-of-sample cross-validation method on voxel-based morphometry (VBM) data. Regions of interest from the paralimbic system, identified in an independent forensic sample, were successful in differentiating youth groups. Models seeking to classify incarcerated individuals to have high or low psychopathic traits achieved 69.23% overall accuracy. As expected, accuracy increased in models differentiating healthy controls from individuals with high psychopathic traits (82.61%) and low psychopathic traits (80.65%). Here we have laid the foundation for using neural correlates of personality traits to identify group membership within and beyond psychopathy. This is only the first step, of many, toward prediction models using neural measures as a proxy for personality traits. As these methods are improved, prediction models with neural measures of personality traits could have far-reaching impact on diagnosis, treatment, and prediction of future behavior.

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### 46 Introduction

Finding patterns in large and sometimes noisy data sets with classification models has become more common. Internet search engines, facial recognition software, and exploring big data are all examples of classification models used to identify patterns in data. As these models become more and more accurate, researchers seek to develop models predicting a specific outcome for a single participant. Considering the complexity and difficult nature of such an endeavor, it may take years for science to develop the theoretically possible highly accurate

prediction models of a single participant. Prediction at the level of an individual may be most useful in a few areas with heterogeneous and comorbid clinical diagnoses. Here we take an initial step toward fine-tuning prediction models with the purpose of affecting positive, individual outcomes.

As several classification models have become more and more prevalent, accuracy in distinguishing groups of individuals has increased. Models discriminating healthy subjects from patients with severe mental illnesses have demonstrated promise, including schizophrenia (Arbabshirani et al., 2013; Schnack et al., 2014; Silva et al., 2014; Sui et al., 2009; H. Yang et al., 2010), bipolar disorder (Schnack et al., 2014), psychosis (Arribas et al., 2010; Calhoun et al., 2008; Sun et al., 2009), and Huntington's disease (Rizk-Jackson et al., 2011). Also, models have been used to predict brain maturation (Dosenbach et al., 2010), substance use (Fan et al., 2006; Pariyadath et al., 2014; Zhang et al., 2005), and substance use outcomes (Marhe et al., 2013; Steele et al., 2014). Clinical diagnosis such as depression (Habes et al., 2013)

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and obsessive–compulsive symptoms (Weygandt et al., 2012a, 2012b) have also been successfully differentiated with prediction models. Each of these prediction models were designed to reduce subjectivity in distinguishing groups by including neuroimaging, genetics, and/or clinical assessment data. In many cases, these models are developed to distinguish between groups that are quite different from each other. A more nuanced discrimination between individuals would be to distinguish individuals on their severity of a specific personality trait or cluster of traits. This is challenging because personality traits often overlap with one another and with other comorbid conditions. Nevertheless, identifying neural correlates of a personality trait could prove more sensitive to differentiating individuals on that trait compared to using other proxy assessments, like self-report or expert-rater assessments.

A well-known and thoroughly examined personality trait is psychopathy, a serious personality disorder characterized by affective and behavioral symptoms. Just less than 1% of the general population is estimated to meet the established clinical criteria for psychopathy, although the rate increases to 15–25% in incarcerated settings (Hare, 2003). Hare's Psychopathy Checklist-Revised (PCL-R; Hare, 2003) is the most common and validated instrument for assessing psychopathic traits in adult forensic settings. Identifying individuals with elevated psychopathic traits may be most beneficial in helping to assign treatment options that are effective (Caldwell, 2011; Caldwell et al., 2007) and not counterproductive (Rice and Harris, 1997). Psychopathic traits, known as callous and unemotional traits and conduct disordered traits (CU/CD) in youth, is most commonly assessed in juvenile forensic populations using the Hare Psychopath Checklist: Youth Version (PCL:YV (Forth et al., 2003), a downward extension of the adult Hare PCL-R. Research has shown that the PCL:YV identifies youth at the highest risk of committing serious and violent crimes as adolescents and/or adults (Davidson et al., 2000; Hawkins et al., 1998, 2000). Psychopathic traits, at least at low to moderate levels, detected early in life often decrease naturally (Frick et al., 2003; Lee et al., 2009; Lynam et al., 2007). However, for a subsample of youth with elevated psychopathic traits, the disorder appears to remain stable across development (Blonigen et al., 2006; Frick et al., 2003; Lynam et al., 2007; Obradovic et al., 2007) and are referred to as being on the "life-course persistent" trajectory (Moffitt, 1993). Identifying risk factors specific to individuals with a life-course persistent trajectory could become useful when assigning treatment or potential long-term risk.

Individuals with elevated psychopathic traits, young and old, have exhibited cognitive and structural deficits originating in paralimbic areas (Kiehl, 2006). A growing body of literature supports this paralimbic hypothesis suggesting individuals with elevated psychopathic traits exhibit aberrant structure (specifically reduced grey matter volume and density) and function in many regions: anterior cingulate cortex (ACC), bilateral amygdala, bilateral hippocampus, medial orbitofrontal cortex (mOFC), bilateral orbitofrontal cortex (OFC), bilateral parahippocampus, posterior cingulate cortex (PCC), and bilateral temporal pole (Fig. 1). Adults and youth with elevated psychopathic traits exhibit similar paralimbic neural dysfunction (Blair, 2006; Budhani and Blair, 2005; Cope et al., 2014; Ermer et al., 2012, 2013; Harenski et al., 2014; Kiehl, 2006; Lockwood et al., 2013; Marsh et al., 2008; Motzkin et al., 2011; Raine et al., 2003). Deficits appear to be specific to the orbitofrontal cortex (Budhani and Blair, 2005; Cope et al., 2014; Ermer et al., 2013), insula (Lockwood et al., 2013), amygdala (Harenski et al., 2014; Marsh et al., 2008), PCC (Ermer et al., 2013), parahippocampal gyrus (Ermer et al., 2013), and ACC (Cope et al., 2014; Ermer et al., 2013; Marsh et al., 2008).

Well-established structural differences have been identified between adults and youth with and without elevated psychopathic or CU/CD traits. A combination of these structural differences may prove more sensitive to differentiating individuals with and without elevated psychopathic traits than other measures. Therefore, as a proof of concept, we develop prediction models with well-established a priori regions of interest (ROI) of structural data alone to identify levels of psychopathic traits by comparing incarcerated individuals with

elevated psychopathic traits, incarcerated individuals with low psychopathic traits, and healthy controls. If successful, a framework will be established to identify neural correlates of many personality traits. Potentially, neural measures of personality traits could yield precise measures of the trait and therefore be practically useful in assessing that trait at an individual level.

Support vector machine (SVM) learning models are developed to separate groups with an out-of-sample cross-validation method. In these models, we use voxel-based morphometry (VBM) data extracted from paralimbic regions of interest (Ermer et al., 2013; Kiehl, 2006) known to be aberrant in individuals with elevated psychopathic traits. It is hypothesized prediction models will be able to differentiate groups using only the VBM ROIs. Once there is evidence that simple VBM ROI analyses are sufficient to separate groups, more sophisticated methods will be employed to refine future prediction models. Predicting levels of psychopathic traits in an individual with precision could have far-reaching impact on diagnosis of other personality traits, treatment, and potential future behavior.

## Methods

### Participants

These data were drawn from the National Institute of Mental Health (NIMH)-funded SouthWest Advanced Neuroimaging Cohort, Youth Sample (SWANC-Y), collected between June 2007 and March 2011, from ongoing research studies at a maximum-security youth detention facility in New Mexico. The present study reports on a subsample of these participants (all males;  $n = 143$ ) for whom structural MRI and the Hare Psychopath Checklist: Youth Version (PCL: YV) (Forth et al., 2003) data were available (mean age = 17.29 years, standard deviation (SD) = 1.19). Using NIH racial and ethnic classification, 19% of the sample self-identified as White, 21% as Black/African American, 6% as American Indian, 36% as Other, 56% as Hispanic, 38% as not Hispanic, and 17% chose not to respond. The sample was primarily (89%) right handed. We selected individuals who scored at or above the clinical threshold of 30 on the PCL: YV ( $n = 71$ ; mean = 32.78; SD = 2.23; range 30–38) and at or below 20 ( $n = 72$ ; mean = 16.25; SD = 3.46; range 2–20). In addition, we report data from male healthy adolescent non-offender healthy controls drawn from the community ( $n = 21$ ; mean age = 17.52 years, SD = 2.53). Using NIH racial and ethnic classification, 47.62% of the sample self-identified as White, 14.29% as Asian, 38.10% as Other, 38.10% as Hispanic, and 61.90% as not Hispanic. The healthy sample was primarily (91%) right handed.

This research was approved by the University of New Mexico Health Sciences Center Human Research Review Committee, and all individuals volunteered to participate after providing written informed consent (if  $\geq 18$  years or age) or after providing written informed assent and parent/guardian written informed consent (if  $< 18$  years of age). Participation did not affect institutional status (e.g., security level, privileges, parole, or release date). Individuals were excluded from participation if they had a history of seizures, epilepsy, psychosis, traumatic brain injury (TBI), other major medical problems, or failed to show fluency in English at or above a grade four reading level.

### Assessments

Trained researchers administered assessments to each participant. These assessments included a measure of psychopathy (PCL: YV), intelligence quotient (IQ), and a TBI questionnaire. All offenders were assessed for psychopathy (i.e., callous and unemotional traits and impulsive/antisocial behaviors) using the expert-rater Psychopathy Checklist: Youth Version (Forth et al., 2003). The PCL: YV assessment includes a review of institutional records and a semi-structured interview that reviews individuals' school, family, work, and criminal histories, and their interpersonal and emotional skills. Individuals are scored on

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