Molecular Psychiatry
https://doi.org/10.1038/s41380-019-0386-4

CORRESPONDENCE

Heterogeneity matters: implications for Poeppl et al.'s (2019) meta-analysis and future neuroimaging research on psychopathy

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Received: 22 August 2018 / Revised: 1 February 2019 / Accepted: 14 February 2019

We applaud Poeppl et al. [1] for their review of the functional neuroimaging literature on psychopathic personality (psychopathy), which provides a useful perspective on the neural correlates of this condition as operationalized by total symptom scores. Nonetheless, several limitations constrain the interpretability of their results and conclusions. Although these limitations include a failure to distinguish among alternative measures of a target construct (i.e., psychopathy) and collapsing across non-interchangeable dependent measures (i.e., MRI–brain activations from different tasks), we focus on one issue of specific relevance to psychopathy: the authors' treatment of this condition as a unitary construct, largely neglecting its heterogeneity. This issue casts doubt on their assertions that certain neural activation patterns are "pathognomonic" of psychopathy, and that their findings may bear implications for pharmacological interventions.

Although certain measures of psychopathy exhibit a higher-order unidimensional structure, other widely used measures, including the Psychopathic Personality Inventory (PPI)—employed in several studies in Poeppl et al.'s meta-analysis—do not. Furthermore, growing evidence suggests that psychopathy, regardless of operationalization, is multidimensional or multi-faceted at a lower-order level [2]. That is, factor-analytic studies reveal distinct subdimensions ("factors" or "facets") underpinning most psychopathy inventories [3], including those heavily represented in Poeppl's meta-analysis. As discussed below, these subdimensions show contrasting associations with a wide array of criterion variables, including electrocortical and neuroimaging measures.

Furthermore, factor analyses of the Psychopathy Checklist-Revised (PCL-R), used in 21 of the 28 studies considered by Poeppl et al., have consistently yielded a multi-dimensional structure at a lower-order level [4]. Early studies revealed two moderately correlated factors, with factor 1 reflecting interpersonal and affective features and factor 2 impulsive lifestyle and antisocial behavior features. More recent research has subdivided these factors into lower-order facets reflecting interpersonal, affective, impulsive lifestyle, and antisocial features. The self-report inventories included in the authors' meta-analysis ($k = 7$) similarly contain distinctive subdimensions.

Still, internal structural analyses of item sets can provide only preliminary evidence of content heterogeneity, in part because non-substantive influences such as similarity in wording or directionality of items can drive factor structure. Distinct patterns of relations with criterion variables can provide more compelling evidence for heterogeneity. In the case of the PCL-R and other psychopathy inventories, subdimensions identified through internal structural analyses frequently exhibit contrasting, and in some cases opposing, relations with external criteria [5]. The affective-interpersonal features typically show positive and negative correlations with social dominance and distress-proneness, respectively. In contrast, the impulsive-antisocial features tend to show positive associations with distress-proneness, as well as with disinhibitory traits. Contrasting associations for these two components of psychopathy have also been found for a range of behavioral and brain-based outcomes. These findings impose important boundary conditions on studies of the neural correlates of global psychopathy scores.

Diverging associations for psychopathy subdimensions are especially pronounced when accounting statistically for the variance shared between them—with cooperative suppressor effects (enhanced relations in opposing directions when controlling for statistical overlap) frequently evident in predicting negative-emotional traits, anxious-depressive

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Published online: 04 March 2019

symptoms, and suicidality. Indeed, in contrast to most psychological domains, such as intelligence testing, in which suppressor effects have been notoriously absent or difficult to replicate when present [6], cooperative suppressor effects for psychopathy subdimensions in predicting external criteria have emerged in numerous studies [3]. Such effects provide compelling evidence for the presence of distinctive constructs embedded within measures.

Given these contrasting associations, individuals attaining high scores on the PCL-R are heterogeneous with regard to traits, overt behaviors, clinical outcomes, and brain and other physiological responses. Evidence also exists for distinct subgroups of individuals identified as psychopathic using the PCL-R, the PPI, and other widely used psychopathy measures—in particular, low anxious-assertive and hostile-distressed subgroups corresponding to the distinction between "primary" and "secondary" psychopathy, respectively [7]. The contrasting or even opposing correlates for psychopathy subdimensions are typically obscured when total psychopathy scores are used [4], resulting in an oversimplified or misleading portrayal of patterns of association. A multi-dimensional approach is thus crucial for elucidating psychopathy's neurobiological correlates.

Of direct relevance to Poeppl et al.'s review, considerable evidence points to distinctive and even divergent fMRI-brain correlates of psychopathy subdimensions. For example, in Seara-Cardosa et al.'s [8] study of associations between PCL-R subdimensions and responses to others' pain, the unique variance in affective-interpersonal features was negatively associated with activation in the anterior insula, inferior frontal gyrus, and midcingulate cortex, whereas the unique variance in lifestyle-antisocial features was positively associated with activation in these same regions. Carré et al. [9] found opposing associations between amygdala activation and fear processing—negative and positive, respectively—for PCL-R interpersonal and antisocial facets. Hyde et al. [10] found that amygdala activity was positively associated with the PPI Self-Centered Impulsivity dimension, but not other PPI dimensions. Although these brain regions emerged in Poeppl et al.'s meta-analysis, the specificity of their associations with particular psychopathy facets was obscured because the authors' analysis focused solely on total scores and total-score groupings (i.e., collapsing across subdimensions).

In conclusion, the authors' near-exclusive focus on the correlates of total psychopathy scores qualifies their conclusions, raising questions regarding their claims of "pathognomonic" neural signatures for psychopathy. Firmer conclusions regarding the functional neuroimaging correlates of psychopathy will await finer-grained meta-analyses that account for psychopathy subdimensions. This perspective mirrors a growing recognition of the multi-faceted nature of psychopathology more generally, and the need for more nuanced characterization of uniqueness versus overlap among disorders in studies of their neural correlates.

Compliance with ethical standards

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

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