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Review article

Prefrontal structural and functional brain imaging findings in antisocial, violent, and psychopathic individuals: A meta-analysis

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ABSTRACT

Brain-imaging studies suggest that antisocial and violent behavior is associated with structural and functional deficits in the prefrontal cortex, but there is heterogeneity in findings and it is unclear whether findings apply to psychopaths, non-violent offenders, community-based samples, and studies employing psychiatric controls. A meta-analysis was conducted on 43 structural and functional imaging studies, and the results show significantly reduced prefrontal structure and function in antisocial individuals. Effect sizes were significant for both structural and functional studies. With minor exceptions, no statistically significant moderating effects of sample characteristics and methodological variables were observed. Findings were localized to the right orbitofrontal cortex, right anterior cingulate cortex, and left dorsolateral prefrontal cortex. Findings confirm the replicability of prefrontal structural and functional impairments in antisocial populations and highlight the involvement of orbitofrontal, dorsolateral frontal, and anterior cingulate cortex in antisocial behavior.

Contents

1. Introduction

In the past decade, research on antisocial behavior (aggression, psychopathy, and conduct problems) has identified several environmental, psychological, and social pathways that potentially lead to these behaviors (Holmes et al., 2001; Raine, 2002; Vermeiren et al., 2002). In addition, mounting evidence has shown structural and functional abnormalities in antisocial individuals, and hypotheses have been presented linking antisocial behavior to deficits in the prefrontal cortex, temporal cortex, insula, amygdala, hippocampus/parahippocampus, and anterior/posterior cingulate gyrus (Blair, 2001; Kiehl, 2006; Raine and Yang, 2006). Among these brain

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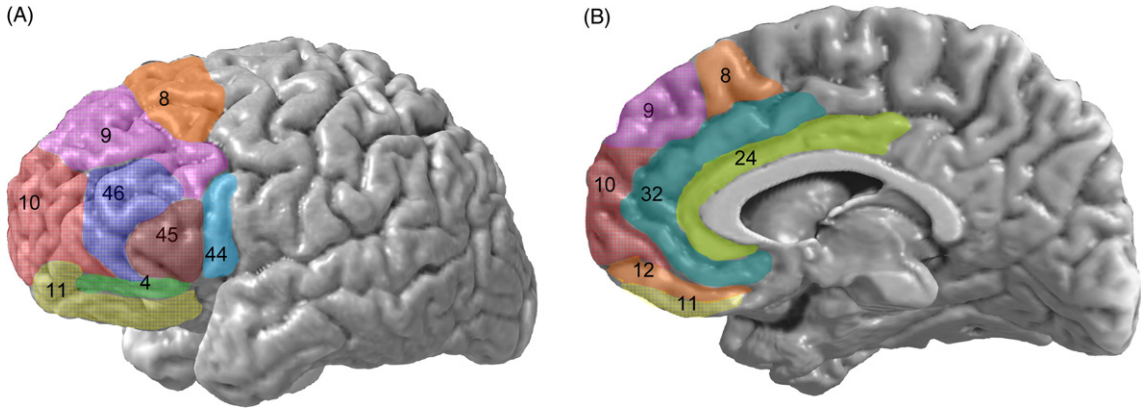

Fig. 1. Lateral (A) and medial (B) illustration of the Brodmann Areas (BA) in the orbitofrontal, dorsolateral prefrontal, ventrolateral prefrontal, medial prefrontal, and anterior cingulate cortices. The orbitofrontal cortex included BA 11, 12, and 47. The dorsolateral prefrontal cortex included BA 8, 9, 10, and 46. The ventrolateral prefrontal cortex included BA 44 and 45. The medial prefrontal cortex included BA 8, 9, 10, 11, and 12. The anterior cingulate cortex included BA 24 and 32.

regions, the prefrontal cortex has been most commonly recognized as the most crucial (although not the only) brain structure to be compromised in violent and antisocial populations (Raine, 1993; Raine and Buchsbaum, 1996; Henry and Moffitt, 1997; Davidson et al., 2000). However, clear interpretation of the literature has proved elusive due to some failures to replicate and some complex findings (e.g., significantly increased rather than decreased activation).

One problem in drawing conclusions from these disparate studies is that most studies treat the prefrontal cortex as one unitary structure based on the fact that it is rich in inter-cortical connectivity, and many areas of functional overlap (Dum and Strick, 1991; Ongur, Ferry, and Price, 2003; Petrides and Pandya, 1999, 2001). However, based on anatomical landmarks, studies have suggested that the prefrontal cortex can be broadly subdivided into the orbitofrontal cortex (OFC), dorsolateral prefrontal cortex (DLPFC), ventrolateral prefrontal cortex (VLPFC), and medial prefrontal cortex (MPFC) (Ongur et al., 2003; Petrides and Pandya, 1999, 2001). Functional studies have also supported such delineation by showing functional specificity of these prefrontal subregions (Bechara, 2004; Campbell, 2007; Volz et al., 2006; Duncan and Owen, 2000; Stuss et al., 2001). Therefore, it is of value to investigate the specificity of any abnormality to prefrontal subregions (Raine and Yang, 2006).

Another important issue concerns whether there are both structural and functional abnormalities in antisocial populations. Despite the fact that studies have shown a correlation between volumetric reduction and decreased brain activation (Johnson et al., 2000; Thomsen et al., 2004), very few if any imaging studies examine both structure and function in the same population. Additional issues that might contribute to variability in findings include heterogeneity in antisocial samples and variation in imaging methodology. Violence, psychopathy, and comorbid psychiatric disorders may moderate study outcomes (Mena et al., 2005; Raine and Yang, 2004; Spampinato et al., 2005; Yang and Raine, 2006). In addition, several imaging methodology variables have been shown to influence quality, including the magnet strength, repetition time (TR), full-width-at-half-maximum (FHWM), and uptake time (Levin and Hoffman, 1999; McCarley et al., 1999), and differences in findings on antisocial behavior could be attributable to these factors.

In order to address these problems, the present meta-analytic review was undertaken to: (a) aggregate the outcomes of all imaging studies on the prefrontal cortex in antisocial individuals, (b) examine the association between antisocial behavior and sub-regions of the prefrontal cortex, (c) evaluate whether such association is more prominent in functional or structural imaging studies, and (d) delineate reasons for variability in previous findings.

2. Method

2.1. Study selection

The search for candidate studies to be included in the meta-analysis was conducted using 35 keywords relevant to antisocial behavior and brain imaging (i.e., Antisocial personality disorder/APD, antisocial behavior, conduct disorder/CD, oppositional defiant disorder/ODD, disruptive behavior disorder/DBD, psychopath, psychopathy, psychopathic, violent, violence, aggressive, aggression, offender, criminal, anatomical magnetic resonance imaging/aMRI, volumetric magnetic resonance imaging/vMRI, diffusion tensor imaging/DTI, structural imaging, functional magnetic resonance imaging/fMRI, magnetic resonance spectroscopy/MRS, perfusion emission tomography/PET, single photon emission computerized tomography/SPECT, functional imaging, prefrontal cortex/PFC) in three electronic indices (PubMed, PsycINFO, ISI Web of Science) for English language studies published between January 1965 and September 2007. In addition, all of the reference lists of the studies included for analysis, as well as several review articles on the relation of brain imaging to aggression and antisocial behavior were reviewed (e.g., Anckarsater, 2006; Brower and Price, 2001; Raine, 2002; Raine and Yang, 2004, 2006; Yang et al., 2008; Yang and Raine, 2008).

To be included in this meta-analysis, the study had to meet all criteria listed below. First, if a group comparison was used, a study had to include at least one antisocial group (defined as a group that contains individuals with APD, antisocial behavior, conduct disorder, oppositional defiant disorder or disruptive behavior disorder, psychopaths, criminals, violent offenders, or aggressive individuals), and one control group of either appropriate psychiatric controls or healthy normal subjects. If correlational analysis was used, a study must have had at least one assessment of antisocial behavior (defined as above). Second, studies had to include one or more of the following imaging methods: aMRI, DTI, fMRI, MRS, PET, or SPECT. Third, the imaging method the study used had to include assessment of either the structure (e.g., volume, neural connectivity) or function (e.g., hemodynamic response, regional cerebral blood flow) of the prefrontal cortex. The prefrontal cortex was defined as the frontal region anterior to the precentral sulcus (primary and association motor areas were excluded). Results found in the following prefrontal sub-regions were also included for region of interest (ROI) analyses: OFC (Brodmann area (BA) 11, 12, 47), DLPFC (BA 8, 9, 10, 46), VLPFC (BA 44, 45), MPFC (medial section of BA 8, 9, 10, 11, 12), and ACC (BA 24, 32) (see Fig. 1). For articles that used a different nomenclature for anatomical regions (e.g., inferior frontal cortex instead of VLPFC), their findings were classified into the four ROIs