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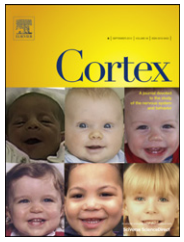

Research report

Inhibitory deficits in the dorsolateral prefrontal cortex in psychopathic offenders

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ABSTRACT

Often typified as cunning social predators, psychopathic offenders show a persistent pattern of impulsive and reckless behavior, the pathophysiology of which has been related to dysfunction in the dorsolateral prefrontal cortex (DLPFC). That is, the DLPFC is important for the regulatory control of impulses and emotion as well as working memory and psychopathic offenders show impairments in all three dimensions. In the present study, we used combined transcranial magnetic stimulation and electroencephalography to compare the physiology of the DLPFC in 13 psychopathic offenders and 15 healthy subjects vis à vis excitability and inhibition. In addition, working memory performance was measured through the letter–number sequencing test. Results showed that compared to healthy subjects, psychopathic offenders had inhibition not excitability deficits in the DLPFC that was accompanied by deficits in working memory performance. In healthy controls and psychopathic offenders working memory performance correlated with the extent of inhibition over the DLPFC. Taken together, these findings suggest that psychopathic offenders suffer from dysfunctional inhibitory neurotransmission in the DLPFC and impaired working memory which may account for the behavioral impairments associated with this disorder.

1. Introduction

Psychopaths are notorious for their callous unemotional personality style and Machiavellianistic use of others. Likely to engage in criminal and aggressive behavior they burden society with enormous costs in addition to inflicting severe emotional harm on their victims (Patrick, 2006). Although psychopathic offenders are capable of executing well-planned crimes (Hervé et al., 2004), they typically act impulsively and do not deliberate the consequences of their actions, neither for themselves nor for others. As reflected in Hare's Psychopathy Checklist-revised second edition (PCL-R:2) (Hare,

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2003) psychopaths display poor behavioral controls, are impulsive and irresponsible and lack the ability to formulate realistic long-term goals (Hare, 2003). In line, Patrick et al. (2009) proposed a tripartite conceptualization of psychopathy in which *meanness*, *boldness* and *disinhibition* are emphasized. According to this conceptualization, disinhibition refers to "impulse control problems, lack of planfulness and foresight, impaired regulation of affect and urges, insistence on immediate gratification and deficient behavioral restraint" (Patrick et al., 2009). Whereas psychopaths may describe this behavior as 'living in the moment' (Babiak and Hare, 2006), in reality these clinical observations point toward cognitive dysfunction, i.e., the incapacity to inhibit impulses and regulate emotion and behavior. Indeed, psychopathic offenders present with higher levels of impulsive-reactive anger (Blair, 2010), response perseverance (Newman et al., 1987), attention deficits (Baskin-Sommers et al., 2011; Newman et al., 2010) and are generally unresponsive to inhibitory information (e.g., potential punishment or negative outcomes) (Zeier et al., 2009). Therefore, psychopathic offenders are thought to exhibit deficits in higher-order cognitive processes (Gao and Raine, 2010; Yang and Raine, 2009) making them vulnerable to a disinhibited antisocial lifestyle.

The dorsolateral prefrontal cortex (DLPFC) is important in the regulation of *emotion and* behavior and is dysfunctional in psychopathy (Rilling et al., 2007; Dolan and Park, 2002), particularly the left DLPFC (Yang and Raine, 2009). Damage to the left DLPFC generates impairments in attention, cognitive flexibility and impulse control that are involved in regulatory control (Yang and Raine, 2009). The authors subsequently suggest that decreased functioning of the left DLPFC in psychopathic offenders can result in antisocial behavior including impulsivity and behavioral disinhibition (Yang and Raine, 2009). The DLPFC is also involved in higher-order cognitive functions such as working memory (Daskalakis et al., 2008b; Smith et al., 1998; Goldman-Rakic, 1995). Working memory involves the online storage and manipulation of information (Barr et al., 2010; Baddeley, 1986) while resisting interference (Kane and Engle, 2003; Kane et al., 2001). Working memory is important for impulse control (Arnsten, 2009), goal-directed behavior (Lepsien et al., 2011) and response inhibition (Chambers et al., 2009). Lower working memory capacity results in less control of emotional responding (Schmeichel et al., 2008) and reduced emotional self-regulation after negative feedback (Schmeichel and Demaree, 2010). Working memory deficits are also correlated with characteristics of secondary psychopathy, i.e., the impulsive antisocial lifestyle (Sadeh and Verona, 2008). Deficits in working memory may therefore result in the impulsive disinhibited behavior and poor emotion regulation observed in psychopathic offenders.

At a neurophysiological level, working memory involves the recruitment of inhibitory interneurons in the DLPFC (Goldman-Rakic, 1995). The phenomenon of cortical inhibition (CI) is defined as the neurophysiological suppression of cortical output neurons by inhibitory interneurons that use γ-aminobutyric acid (GABA) as their primary neurotransmitter (Iversen et al., 1971; Fitzgerald et al., 2009). This form of inhibitory neurotransmission can be quantified with paired pulse transcranial magnetic stimulation (TMS). That is, TMS generates magnetic fields that travel through the cranium to both inhibitory and excitatory interneurons that can, in turn, be measured. Traditionally confined to measurement from motor areas, the combination of TMS with electroencephalography (EEG) has enabled researchers to study inhibitory and excitatory processes from non-motor cortical areas such as the DLPFC (Farzan et al., 2009; Daskalakis et al., 2008b). The advantage of TMS combined with EEG is that it measures real time physiological processes and networks in the brain. GABAergic inhibitory neurotransmission in the DLPFC has been reported to correlate positively with working memory performance (Daskalakis et al., 2008b) and suggests a strong interplay between inhibition in the DLPFC and working memory performance, both of which are important in the control of behavior.

The aim of this study was to assess inhibition and excitability directly from the left DLPFC in psychopathic offenders compared to healthy subjects whilst measuring working memory performance. We hypothesized that psychopathic offenders would demonstrate poorer working memory performance and decreased CI over the DLPFC but not over the motor cortex. In addition, we anticipated that the previously observed relationship between working memory and CI over the DLPFC (Daskalakis et al., 2008b) would be replicated.

2. Methods and materials

2.1. Participants

Thirteen right-handed male psychopathic offenders (age in years: mean ± standard deviation (SD), 34.2 ± 9.2; age range 22–55) and fifteen right-handed (Oldfield, 1971) age-matched healthy male subjects (age in years: mean ± SD, 34.0 ± 9.9; age range 22–51) were enrolled in the study. Psychopathic offenders were recruited through posters displayed in halfway houses in the Greater Toronto Area and through the Law and Mental Health Program at the Centre for Addiction and Mental Health (CAMH). Halfway houses are residential facilities for men on conditional release to the community. Their function is to assist in gradual community reintegration while providing supervision. Thirty-eight violent offenders were interviewed of which twenty-one offenders met criteria for inclusion, although 6 re-offended before they could be included in the study. The thirteen psychopathic offenders that were included scored 25 or higher (mean ± SD, 28.8 ± 3.0) on the PCL-R:2 (Hare, 2003). Offenders were asked to sign a Release of Information after which a review of case notes and psychological assessments was carried out to retrieve the PCL-R score and to exclude co-morbid psychiatric or neurological disorders. Exclusion criteria included age under 18 or over 65, schizophrenia, schizophreniform/psychotic disorders, bipolar disorder, affective or anxiety disorders or any co-morbid personality disorders. Exclusion criteria for all subjects included substance abuse or dependence in the last 6 months determined through the Diagnostic Statistical Manual-IV-TR (DSM-IV-TR). However, 87% of the included psychopaths reported a history of drug use and had previously met criteria for substance use disorder. Drug screening at the halfway houses indicated none of the psychopathic offenders

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