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Neurocognitive elements of antisocial behavior: Relevance of an orbitofrontal cortex account

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Abstract

This paper reviews the role of orbitofrontal cortex (OFC) lesions in antisocial behaviors and the adequacy of a strict OFC account of antisocial disorders where there is no evidence of lesion. Neurocognitive accounts of antisocial behaviors are extended beyond the OFC. Several methodological shortcomings specific to this neuroscience approach to antisocial behavior are identified. A developmental approach is advocated to chart the developmental sequences of impaired brain development and of the various comorbid states typically seen in antisocial disorders.

1. Introduction

Individuals with orbitofrontal cortex (OFC) lesions are typically described as disinhibited, socially inappropriate, misinterpreting others' moods, impulsive, unconcerned with the consequences of their actions, irresponsible in everyday life, underestimating the seriousness of their condition (lack of insight), and showing a poor sense of initiative (Rolls, Hornak, Wade, & McGrath, 1994). The parallels between the effects of OFC lesions on social behavior and the symptoms of antisocial disorders are striking. It is not surprising then that questions about the underpinnings of antisocial disorders have been sought through a frontal lobe account.

2. Accounting for the effects of OFC lesions

This interest goes back as far as the classic case of Phineas Gage. One day, as Gage was working with explosives, a charge was accidentally set off and projected a tamping rod to his head, through his frontal lobe but spared vital brain centers. Although Gage survived the blast, he became irritable, short-tempered, obnoxious, irresponsible, and could no longer hold a job or provide for himself. Nonetheless, neurocognitive functions were purportedly intact. A recent reconstruction of the lesion site with the help of Gage's preserved skull and modern imaging techniques strongly suggests that the lesions were mainly located in the orbitofrontal and ventromedial frontal lobes (Damasio, Grabowski, Frank, Galaburda, & Damasio, 1994). Although not all cases of frontal injuries end up with such a poor prognosis (Mataro et al., 2001) there is considerable literature to warrant poor prognoses. Similar

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observations have been often reported in the literature. For example, aggressive and violent 'attitudes' were higher in a group of US Vietnam war veterans who suffered OFC injuries, than in a normal control group and a group with lesions in other brain sites (although they were also high for a group of mediofrontal lobe patients; Grafman et al., 1996). A similar case with left unilateral OFC damage in adulthood was described as "acquired antisocial personality disorder" (Meyers, Berman, Scheibel, & Hayman, 1992). In this latter case, performance on neurocognitive tests was also unimpaired despite obvious personality changes and inability to maintain an occupation. Because such examples abound several hypotheses about the role of the OFC in behavior regulation were developed. One of these, the "somatic markers hypothesis," suggests that ventromedial frontal lobe lesions impair the capacity to consider emotions when making a decision (Damasio, 1996; Damasio, Tranel, & Damasio, 1991). This impairment leads to disadvantageous consequences, self-defeating behavior, and violations of social norms. Because of this, the resulting syndrome was called "acquired sociopathy" (Damasio, 2000; Damasio et al., 1991). Alternate and often complementary hypotheses suggest that the primary deficit following such frontal lobe lesions lies in self-reflective awareness (Stuss, Gow, & Hetherington, 1992), perspective taking (Stuss, Gallup, & Alexander, 2001), social schema knowledge (Grafman et al., 1996), the ability to respond appropriately to social reinforcers (Rolls et al., 1994), the ability to make inferences about the mental states of others (or a Theory of Mind; Stone, Baron-Cohen, & Knight, 1998), and processing of social cues (Brothers, 2001). Many of these views have been examined in relation not only to acquired psychopathy following brain damage, but also to developmental psychopathy (Blair & Cipolotti, 2000) and antisocial disorders (Bergvall, Wessely, Forsman, & Hansen, 2001).

3. Accounting for antisocial behaviors

Neurocognitive accounts of antisocial behavior also abound. Among these, Moffitt (1990a, 1993) put forward the main theory for a brain–behavior account for the development of antisocial conduct. With the help of longitudinal designs she noted that adolescents with a form of early onset antisocial behavior, which included aggression and hyperactivity, showed poorer neuropsychological test performance than those with a later onset of antisocial behavior problems. This latter group was also less likely to pursue a criminal career in adulthood than the early onset group. Although trajectories of antisocial conduct now appear to be more complex than this two-category model implied (Broidy et al., 2003), those children with a trajectory of early onset persistent antisocial behavior problems do appear to have neuro-cognitive deficits relative to other trajectories (Séguin, Nagin, Assaad, & Tremblay, in press), and these risk factors could be detected as early as in the preschool years (Raine, Yaralian, Reynolds, Venables, & Mednick, 2002; Séguin, 2003). Risk for early onset persistent antisocial behavior also appears to be compounded by a concurrent history of early hyperactivity (Lynam, 1998; Moffitt, 1990a). However, several nomenclatures, one psychiatric, one legal, and one clinical, complicate the study of antisocial behaviors. Although there is overlap between these nomenclatures, there is also considerable heterogeneity within each. The main relevant psychiatric disorders fall into the developmental externalizing disorders of Conduct Disorder (CD), Attention Deficit Hyperactivity Disorder (ADHD), and Oppositional Defiant Disorder (ODD), and the adult

disorder AntiSocial Personality Disorder (ASPD) which requires also an adolescence diagnosis of CD before age 15 (American Psychiatric Association, 2000). Characteristics of delinquents and criminals include fraud, vandalism, theft, bullying, intimidation, arson, cruelty to animals, assault, rape, and homicide. Finally the clinical construct of psychopathy has generated considerable research as well (Hare, Hart, & Harpur, 1991).

A further distinction worth noting is that contrasting reactive (or hostile) aggression to proactive (or instrumental) aggression. Reactive aggression refers to acts caused by attributions of hostile intent to others or distorted interpretations of other's ambiguous behavior as provocative, regardless of the other's intention (Dodge, 1991; Dodge & Coie, 1987; Price & Dodge, 1989). This type of aggression is defined as negatively reinforcing in nature, without a self-generated goal, and is more often impulsive. Conversely, proactive aggression appears to occur without provocation and may comprise coercion, dominance, or bullying. Aggression here is seen as a means to gain a valued outcome and is thus positively reinforcing. Planned aggression is typically proactive. However, this distinction can be problematic due to the high correlation between the proactive and reactive aggression constructs, at least in community samples (Dodge & Coie, 1987; Séguin & Tremblay, 2004). The relation may not be linear however. In a sample of close to 900 boys from low SES background we found that pro-active aggression was almost always associated with reactive aggression, but that reactive aggression was not necessarily associated with proactive aggression (Séguin & Tremblay, 2004). In other words, proactive aggression without reactive aggression is rare in the general population. Nonetheless, proactive aggression predicts later conduct problems even after controlling for reactive aggression (Vitaro, Gendreau, Tremblay, & Oligny, 1998).

The strongest parallels between purported impairments in OFC functions and antisocial behavior have naturally been investigated with the construct of psychopathy (Damasio, 2000; Schmitt, Brinkley, & Newman, 1999).

4. Psychopathy

The evidence for psychopathy is largely reviewed by Blair (see this issue). We will thus summarize a few issues here. Psychopaths are often assessed with the Psychopathy CheckList-Revised (PCL-R; Hare et al., 1991). PCL-R defined psychopaths are studied among criminals and the assessment is based on a complex and thorough examination of official records in addition to an interview. When non-criminals are assessed, their scores on the PCL-R tend to be lower (i.e., below 30—although most criminals also score below 30, and non-psychopathic criminals and control groups typically score below 20). Scores between 20 and 30 may reflect more largely Anti-Social Personality Disorder (ASPD). Self-report instruments have also been used (Lynam, Whiteside, & Jones, 1999), and children with psychopathic tendencies have been studied using various behavior rating systems (Frick, O'Brien, Wootton, & McBurnett, 1994; Lynam, 1998). The PCL-R also yields two to three correlated factors representing behavioral (impulsivity and irresponsibility), emotional (callousness and defective emotional experience), and interpersonal aspects (narcissism, arrogance, and deceitfulness; Cooke & Michie, 2001). The Psychopathy Screening Device applied to children also found three similar factors (Frick, Bodin, & Barry, 2000) and there

is an emerging primate model of psychopathy (Lilienfeld, Gershon, Duke, Marino, & de Waal, 1999). Among criminals, psychopaths tend to be the most violent and recidivistic (Hare, 1999).

Although there have been initial reports of neuropsychological impairments in psychopaths (Gorenstein, 1982), this finding has generally not been replicated (Hoffman, Hall, & Bartsch, 1987; Sutker & Allain, 1987), and these and other studies overwhelmingly conclude that neuropsychological function emphasizing cognitive processes is not different than for non-psychopaths (Hare, 1984; Hart, Forth, & Hare, 1990; Hoffman et al., 1987). A few exceptions are noted in studies where psychopaths were subdivided as a function of anxiety levels (Smith, Arnett, & Newman, 1992)—which is a construct that shares a complex relation with psychopathy (Frick, Lilienfeld, Ellis, Loney, & Silverthorn, 1999; Schmitt & Newman, 1999), or as a function of whether psychopaths tend to be successful or not (i.e., the more successful have better dorsolateral frontal lobe ability; Ishikawa, Raine, Lencz, Bihrle, & LaCasse, 2001). However, the Smith et al. (1992) study found two significant effects (out of 6 expected) for the Block Design subtest of the Wechsler Adult Intelligence Scale and for the Trail Making Test-B after controlling for IQ and substance abuse for a comparison between low anxious psychopaths and low anxious non-psychopaths, but the results were not clear when analyzed in a psychopathy by anxiety factorial design. Of note, Hart et al. (1990) reported a marginally significant effect ($p < .06$) of psychopathy on the TMT-B in one sample. In another study the psychopathy effect was also marginal ($p < .08$) on the Wisconsin Card Sorting Task, a measure typically unaffected by OFC lesions, (Lapierre, Braun, & Hodgins, 1995). In contrast, psychopaths performed significantly poorly on OFC tasks in that same study. Finally, note also that the Ishikawa et al. (2001) study did not use the PCL-R definition of psychopathy. The absence of clear neuropsychological impairments is important for testing an OFC account of psychopathy because localized OFC lesions typically do not affect performance on conventional neuropsychological tests.

Blair and colleagues have conducted a comprehensive program of studies that examine the parallels between acquired sociopathy and developmental psychopathy (Blair, Morris, Frith, Perrett, & Dolan, 2000), in children (Blair, Colledge, & Mitchell, 2001; Fisher & Blair, 1998), and in adults (Mitchell, Colledge, Leonard, & Blair, 2002), in addition to examining emotional processing in normal controls (Blair et al., 2000), in psychopathic children (Blair et al., 2001; Stevens, Charman, & Blair, 2001), adults (Blair, 2001), and in patients with OFC lesions (Blair et al., 2000). One problem noted in this literature is a difficulty for psychopaths in shifting a dominant behavior when contingencies have been reversed. If that dominant behavior is antisocial in nature, an objective change in contingencies will not help alter the ongoing course of action. These response reversal impairments can be found, amongst others, in several studies of Newman and colleagues who propose a septohippocampal model to explain failures in the response modulation of goal-oriented action (Newman & Lorenz, 2002). The parallels between psychopathy and acquired psychopathy are based on the similarity of their performances on the Iowa Gambling Task (Bechara, Damasio, Damasio, & Anderson, 1994; see also Bechara this issue), and the Intradimensional/extradimensional shift task (Downes et al., 1989). However, in considering the limitations of an OFC account of psychopathy, Blair and colleagues note that the

characteristics of psychopathy and patients with OFC lesions do not overlap entirely. As a general principle, it is important to distinguish antisocial behavior that emerges following some form of head trauma in individuals without prior histories of antisocial behavior, and a long history of antisocial behavior without evidence of brain trauma. In this respect it is often noted that psychopaths are more likely to show physical violence than non-psychopath criminals (Hare, 1999), whereas there is little evidence that patients with OFC lesions are physically violent (Grafman et al., 1996). As a further distinction, the aggression of OFC patients tends to be reactive/hostile in contrast to that of psychopaths which is arguably more proactive/instrumental (Blair et al., 2000). However, among offenders, psychopathy scores were found to be higher in offenders who had a history of at least one instrumental offence (Cornell et al., 1996). Thus although psychopaths could show both reactive and proactive aggression (Cornell et al., 1996), psychopaths are particularly characterized by proactive aggression while OFC patients would show almost exclusively reactive aggression.

5. Limitations to a strict OFC account of psychopathy

A strict OFC account of psychopathy has to be reconsidered. Mitchell et al. (2002) emphasize the complementary role of the amygdala in a circuit that is key to assigning motivational value to stimuli. In fact they suggest that amygdala dysfunction may predate OFC impairments as only amygdala function seems impaired in children with psychopathic tendencies whereas both amygdala and OFC functions appear impaired in adult psychopaths (Mitchell et al., 2002). This proposition is partly based on findings of poor fear-recognition (and sadness, to some extent) in individuals with amygdala lesions and in psychopaths (Blair et al., 2002). However, the experience of negative affect, including fear and sadness, would be preserved in patients with lesions to the amygdala, whether these lesions are unilateral or bilateral (Anderson & Phelps, 2002). This highlights a dissociation between appraisal of fearful expressions in others and the subjective experience of fear (Anderson & Phelps, 2002). Psychopaths, however, also show lack of fear (Herpertz et al., 2001). In contrast, individuals suffering from social phobia show increased amygdala activation (Stein, Goldin, Sareen, Zorilla, & Brown, 2002). Because amygdala deficits may be developmental in psychopaths, their lack of experience in fear recognition may reduce their ability to appraise cues for fear (see Blair this issue). Nonetheless, the role of the amygdala in aggression in general may be complex because it is also considered to be involved in impulsive aggression (which is not necessarily incompatible with an involvement in proactive aggression more prevalent in psychopaths) as part of a circuit implicating the amygdala, OFC, and anterior cingulate (Davidson, Putnam, & Larson, 2000), and in the impulsivity of Borderline Personality Disorder (Driessen et al., 2000).

Finally the empirical bases of an OFC account of psychopathy rely mainly but not exclusively on the Iowa Gambling Task (Bechara et al., 1994), and the Reversal Learning phase of the Intradimensional/extradimensional shift task (Downes et al., 1989). Both tasks have recently been shown not to be sensitive to lesions circumscribed to the OFC in the way it had been thought previously (Manes et al., 2002). In fact, although OFC lesions were thought to increase impulsivity on the Iowa Gambling Task, the contrary was found: Patients with lesions circumscribed to the OFC performed equally well as controls and were actually slower at making decisions (Manes et al., 2002). Poor performance on the Iowa Gambling

Task was found in patients who had large lesions that included the OFC. This would be consistent with the extent of lesions found in earlier studies (Bechara et al., 1994; Bechara, Tranel, Damasio, & Damasio, 1996). Efforts at finding patients with circumscribed lesions have led to further discoveries that will necessarily lead to revisions of current models. For example, it has also recently been shown that only the right but not the left ventromedial prefrontal cortex might be implicated in poor performance on the Iowa Gambling Task and in abnormalities of emotion processing and personality (Tranel, Bechara, & Denburg, 2002).

6. Brain imaging structure and function in other antisocial disorders

In addition to psychopathy several disorders of self-regulation have been the object of neuropsychiatric investigations (Driessen et al., 2000; Eliez & Reiss, 2000). Other studies of brain function and structure in a variety of antisocial disorders have been conducted. These have not specifically examined OFC function or psychopathy. For example, ‘frontal dysfunctions’ were found in 65% of murderers (Blake, Pincus, & Buckner, 1995). In another study, violent adolescent and adult psychiatric patients compared with non-violent controls have been shown to exhibit reduced overall pre-frontal activity and increased anterior medial prefrontal activity (Amen, Stubblefield, Carmichael, & Thisted, 1996).

One particular set of studies was undertaken by Adrian Raine and colleagues at UCLA on a heterogeneous group of suspected murderers pleading not guilty by reason of insanity (SMPNGRI). In a first study they found reduced activity circumscribed to the anterior left pre-frontal cortex while performing the Continuous Performance Task (CPT), a measure of sustained attention (Raine et al., 1994). Lower prefrontal function was found in individuals who had committed impulsive murders as opposed to planned murders. If we follow the reactive-proactive aggression distinction drawn earlier, this would suggest lower frontal function in reactive aggression. A following study compared the SMPNGRI who had a history of psychosocial deprivation (abuse or neglect) to those without such a history (Raine, Phil, Stoddard, Bihrle, & Buchsbaum, 1998). Prefrontal functional deficits were more severe in non-psychosocially deprived murderers. This provides strong support for a biological vulnerability for violence in that group. In another study Raine and colleagues (Raine, Lencz, Bihrle, LaCasse, & Coletti, 2000) also show an average 11% reduction in frontal cortex gray matter in ASPD.

7. Studying aggressive processes in non-aggressive individuals

The involvement of orbital and ventral areas of the frontal lobe in aggressive conduct have also been examined in non-aggressive individuals (Pietrini, Guazzelli, Basso, Jaffe, & Grafman, 2000). Participants were instructed to use mental imagery scenarios during a brain imaging session, a common technique used in brain imaging research. The scenarios varied in level of provocation and in restraint imposed to the participant. Thus a participant was instructed to imagine taking an elevator ride with his mother and two strangers. One ride is uneventful (no provocation–no restraint). However, at high provocation, the strangers attack the mother, and the participant’s level of imaginary restraint is varied from high (passive observation) to low (severe violent retaliation). Results show that emotional reactivity was higher, but ventromedial frontal cortex activity was lower in all of the aggressive conditions,

and it was lowest in the unrestrained aggression condition. This was taken as evidence that the ventromedial frontal cortex played an inhibitory role that varied inversely as a function of restraint imposed.

8. Neuropsychological studies of antisocial behaviors

A historically antecedent approach to brain imaging is one that measures performance in a variety of domains and situations to draw inferences about brain function. Among the neurocognitive approaches to antisocial behavior problems, neuropsychological studies have been the most common and most affordable even in the context of recent advances in brain imaging studies. The neuropsychology of antisocial disorders has been the object of several reviews since Moffitt (1993) developed her theoretical work in the context of critical reviews of the neuropsychology of delinquency (Moffitt, 1990b) and of conduct disorder (Moffitt, 1993; see also Pennington & Bennetto, 1993). A number of other significant reviews were published around that time and in the years that followed (Giancola, 1995; Kandel & Freed, 1989; Morgan & Lilienfeld, 2000; Teichner & Golden, 2000). Moffitt (1990b) initially identified deficits in three specific areas: language abilities, executive function, and cerebral dominance. A considerable amount of research has focused on the construct of executive function. Executive function is a key component for the self-regulation of thought and action and emphasizes cognitive processes associated with problem solving (Zelazo, Carter, Reznick, & Frye, 1997). Related processes involve inhibition control, working memory, as well as language and general memory abilities. Executive function is largely, but not exclusively, mediated by the frontal lobes.

In order to investigate executive function in antisocial conduct we chose to study physical aggression, a specific form of antisocial behavior that cuts across many categories. This is arguably the most damaging and feared form of antisocial behavior. We used a developmental perspective and based our definition of the phenotype on repeated measurements of physical aggression by teachers during childhood and adolescence. We also rated hyperactivity because of its high comorbidity with antisocial behavior problems in general and because of the important literature on executive function problems in hyperactive children (Pennington & Ozonoff, 1996). Regulation of motor response is common to both physical aggression and hyperactivity.

In a series of studies that contrasted executive function, verbal abilities, and tests of cerebral dominance, we found that working memory was poorest in boys with a history of physical aggression even after controlling for non-executive abilities relevant to executive function, IQ, and ADHD (Séguin, Boulerice, Harden, Tremblay, & Pihl, 1999; Séguin, Pihl, Harden, Tremblay, & Boulerice, 1995). The constructs of reactive and proactive aggression do not specifically include physical aggression (Dodge & Coie, 1987) and were not related with history of physical aggression in this sample (Séguin & Tremblay, 2004). The working memory tests we have used were the Self-Ordered Pointing test and a number randomization test (mid-dorsolateral frontal lobe) and conditional association tasks (posterior dorsolateral frontal lobe; Petrides, Alivisatos, Evans, & Meyer, 1993; Petrides, Alivisatos, Meyer, & Evans, 1993). Whereas our studies were conducted in boys, other studies have also found a negative association between executive function and physical aggression after controlling for

ADHD in girls as well (Giancola, Mezzich, & Tarter, 1998). Poor working memory would affect all stages of executive function. Thus hostile biases in appraising a problem would be difficult to reconsider, plans would be difficult to carry out, rules (even if they are well known) would be difficult to apply in real time, and monitoring of a plan (detection and error correction) would be difficult to achieve.

9. Methodological issues in neurocognitive studies of antisocial disorders

Prior to this series of studies, the literature had been quite ambiguous about the role of executive processes in aggression (Pennington & Ozonoff, 1996). There may be two reasons accounting for that. First, studies typically examined conduct problems, which may or may not have included physical aggression. Second, they may not have used a comprehensive assessment of executive function with well-validated tests. Third, executive function is a complex construct involving several dissociable abilities (Robbins, 1996) and using one test of a component of executive function cannot be claimed to be a test of the entire construct (Amen et al., 1996). Thus, there may have been a lack of sensitivity and specificity of measurement in several studies that failed to find the expected relations.

Other neurocognitive studies supporting a role for frontal processes in antisocial disorders abound. However, as most studies do, they suffer from some methodological shortcomings. For example, violent offenders were also shown to be considerably impaired on both attentional set shifting and reversal abilities (Bergvall et al., 2001). Relative to the data presented earlier on psychopaths, the attentional set shifting impairment was considerably more severe. So it may be unlikely that these criminals were psychopathic. However, these criminals generally had a long history of behavior problems, showed considerable comorbidity with psychiatric personality disorders and were also heavily medicated. In another study, ASPD individuals were described in terms of psychopathic traits and performed on OFC tests similarly to psychopaths in the PCL-R sense of the term (Dinn & Harris, 2000). However, the constructs of psychopathy and ASPD, despite considerable overlap, remain nonetheless different.

Thus one particularly problematic feature of antisocial behavior problems, besides being somewhat heterogeneous, is comorbidity with several disorders (Arseneault, Moffitt, Caspi, Taylor, & Silva, 2000a). Many of these disorders feature an ‘impulsive’ component such as drug abuse (Bechara & Damasio, 2002; Bechara et al., 2001; London, Ernst, Grant, Bonson, & Weinstein, 2000; Paulus et al., 2002), acute alcohol intoxication (Giancola, 2000a, 2000b; Mazas, Finn, & Steinmetz, 2000), early onset forms of alcohol abuse (Laakso et al., 2002), and pathological gambling (Cavedini, Riboldi, Keller, D’Annucci, & Bellodi, 2002). Antisocial behavior can also be comorbid with other mental illnesses, such as bipolar disorders (Clark, Iversen, & Goodwin, 2001), schizophrenia (Chemerinski, Nopoulos, Crespo-Facorro, Andreasen, & Magnotta, 2002; Hutton et al., 2002; Nolan, Volavka, Mohr, & Czobor, 1999), schizophrenia spectrum disorders (Arseneault et al., 2000a), depressive states even after remission (Bremner et al., 2002), and ADHD (Colledge & Blair, 2001). However, these conditions in themselves are not necessarily risk factors for antisocial behavior. Such a case has been made for ADHD, for example (Farrington, 2000; Farrington & Loeber, 2000; Nagin & Tremblay, 1999; Stouthamer-Loeber, Loeber, Wei, Farrington, &

Wikstrom, 2002). Psychopathy is mainly related to alcohol and drug abuse (Hemphill, Hart, & Hare, 1994; Mailloux, Forth, & Kroner, 1997; Smith & Newman, 1990), inversely related to depression (Stalenheim & von Knorring, 1996), the callous/unemotional component of psychopathy appears to be unrelated to ADHD (Colledge & Blair, 2001), and the base-rate for psychopathy in a schizophrenia population was similar to that of a normal population (Nolan et al., 1999). Nonetheless, one particularity of poor frontal lobe functions is that they have been implicated in all of these comorbid conditions, although some may be predominantly dorsolateral frontal rather than OFC. This indeed plagues the majority of the study designs of antisocial individuals reviewed herein. To complicate matters, OFC problems are also found in disorders not readily associated with antisocial behavior such as Obsessive–Compulsive Disorder (Cavedini et al., 2002; see also Evans, Lewis, and Iobst, this issue). Further, underlying some of these disorders may be deficient serotonin regulation, which has been involved in OFC function in studies of aggressive individuals (Ranganath, Johnson, & D'Esposito, 2002), as well as in performance on measures sensitive to OFC function (Rogers et al., 1999; Rogers et al., 2002), and in fear-recognition, related to amygdala function (Hamer, Rogers, Tunbridge, Cowen, & Goddwin, 2003).

Is it likely that these studies are assessing a single common component? There is indeed a common antisocial thread throughout many of these behavior problems (repeated engagement in high-risk behavior with immediate rewards and long term adverse consequences for the self and others). However, most of these studies have only assessed a restricted range of behavior problems, which makes them difficult to compare and contrast. Therefore the question remains unanswered.

The absence of group differences on neuropsychological test scores may be misleading. This can be illustrated by two examples. First, Raine and colleagues noticed a lack of group differences on the performance of a sustained attention task, but a group difference in the neural circuits underlying performance on that task (Raine, Buchsbaum, & LaCasse, 1997). In other words between-groups neuropsychological test scores may not differ quantitatively, but the processes underlying such performance would differ qualitatively. Whether Raine and colleagues identified compensatory mechanisms for sustained attention task performance or the actual network underlying antisocial behavior is a different question. Second, we have recently noted a similar phenomenon when we studied performance on the one-deck card-playing task (considered to be a reversal task; Siegel, 1978). In this task, an incentive to turn cards is initially frequently rewarded. As losses gradually increase, an optimal strategy is to stop before losses get too great. We found an absence of group differences in number of cards played between two groups of physically aggressive boys, one with a stable history of elevated levels of physical aggression, the other with an unstable history of physical aggression (Séguin, Arseneault, Boulerice, Harden, & Tremblay, 2002). Although both groups perseverated significantly more than a non-aggressive group, the poor performance of the unstable group appeared to be mediated by their difficulties in emotion regulation (i.e., Neuroticism; Eysenck & Saklofske, 1983), whereas emotional regulation could not explain the performance of the stable aggressive boys. These observations were interpreted in the context of a theory that posits at least two pathways to deficient self-regulation, one based on a difficulty in regulating emotions and the other on a fundamental information processing deficit (Newman & Lorenz, 2002). These two examples illustrate the

complexity we must consider, and absence of quantitative group differences on a task may not be the whole story. It will become more and more important to better understand the processes that underlie task performance and consider an evaluation of those processes in future studies.

10. Developmental issues

One significant distinction was drawn between antisocial behavior that emerges following some form of head trauma in individuals without prior histories of antisocial behavior, and individuals with a long history of antisocial behavior without evidence of brain trauma. Between these two extremes are individuals with a long history of antisocial behavior that could have been the result of early brain trauma. Such brain trauma could have been caused by pregnancy or birth complications, a history of exposure during or after pregnancy to brain altering psychopharmacological agents (i.e., cigarette smoke, alcohol, and drugs), traumatic experiences (i.e., abuse), or by behavior problems that heightened the risk of head trauma through accidents or fights (i.e., hyper-activity and oppositional defiant).

A decade ago only a few case studies of early pre-frontal injury and behavior had been published (Eslinger, Grattan, Damasio, & Damasio, 1992). However, several new studies have emerged since (see Eslinger, Flaherty-Craig, & Benton in this issue; see also Stuss & Anderson, this issue). The lesions documented in these studies reliably lead to chronic adaptation problems that resemble developmental psychopathy (Anderson et al., 1999; Eslinger, Biddle, Pennington, & Page, 1999; Eslinger & Grattan, 1991). As we have shown above, the resemblance with actual psychopathy remains limited. Physical aggression was also rarely observed. A noted exception is one case study where, despite normal IQ and general memory abilities, early bilateral frontal damage was associated with assault (Price, Daffner, Stowe, & Mesulam, 1990). Other early developmental characteristics may also increase the likelihood of antisocial behavior. Minor physical anomalies, which may reflect subtle fetal development complications that could affect brain development, clearly increase risk for physical violence in late adolescence (Arseneault, Tremblay, Boulerice, Séguin, & Saucier, 2000b). Similar results were found for obstetrical complications (Arseneault, Tremblay, Boulerice, & Saucier, 2002). Maternal smoking during pregnancy has been related to externalizing disorder problems (i.e., CD, ADHD, and ODD) in childhood (Breslau & Chilcoat, 2000; Orlebeke, Knol, & Verhulst, 1999; Weissman, Wickramaratne, & Kandel, 2000), and into adulthood (Rasanen et al., 1999), as well as poor neurocognitive function in children (Eskenazi & Castorina, 2000). Maternal smoking during pregnancy was also related to number of conduct symptoms in the parents, which suggests a complex intergenerational transmission process (Zoccolillo, 2000). Several of these issues have been reviewed recently as significant modulating factors of a developmental theory of frontal lobe deficits (Raine, 2002a).

Also about a decade ago, Moffitt noted that neurocognitive accounts were not very impressive univariate predictors of conduct problems; they probably work in the context of interactions between person and environment over the course of development (Moffitt, 1993). Since Moffitt's earlier remarks a growing number of studies show that, unless one considers interactions with key modulating factors, such as those reviewed at the beginning

of this section, one may miss important effects entirely. For example, although lesions such as those suffered by Phineas Gage led to severe psychosocial maladaptation, there also cases where such lesions have occurred and for which the outcome was more stable, perhaps because of a supportive environment (Mataro et al., 2001). In a recent paper Raine reviewed 39 examples of such biosocial interactions in the study of antisocial and violent behavior across the life span (Raine, 2002b). In our own work we found that minimal physical anomalies and birth complications increased the risk for violent delinquency in interaction with early psychosocial adversity (Arseneault et al., 2002; Arseneault et al., 2000b). By adversity we mean low family income, poor education, low occupational status, and being raised by a single parent. Low adversity could be considered a protective factor.

One way to sort out the developmental sequence of the various comorbid disorders described above (CD, ADHD, ODD, depression, Bipolar Disorder, OCD, schizophrenia, drug, alcohol abuse, and other effects of an early onset antisocial lifestyle, or the effects of minimal brain damage) is through large longitudinal studies that begin in early childhood, preferably during pregnancy. Such studies are currently multiplying and producing fascinating results (Broidy et al., 2003; Caspi et al., 2002; Olds et al., 1997; Tremblay et al., 1999; Tremblay et al., in press; Tremblay, Vitaro, Nagin, Pagani, & Séguin, 2003). In our own work we have applied formal statistical techniques (Nagin, 1999) to teacher-ratings of physical aggression and hyperactivity throughout childhood and adolescence (Nagin & Tremblay, 1999). This method identified trajectories of behavior across time and was applied to six international samples (Broidy et al., 2003). Of note, across all samples, and despite different methods of identifying physical aggression, emerged one group of about 4–5% of children that was fairly high in physical aggression over time. We have examined high trajectories of aggression and hyperactivity from kindergarten to age 15 and found considerable impairment in working memory as a function physical of aggression only even after controlling for other neuropsychological dimensions and IQ (Séguin et al., in press).

A large cross-sectional study of the Canadian population of children 0–11 years also revealed that physical aggression peaks at about age $2\frac{1}{2}$ years and then gradually declines over time (Tremblay et al., 1997). However, as seen in the other studies spanning childhood and adolescence, there seems to be a small group that fails to develop the necessary self-regulatory skills required for controlling their violence. We have therefore developed a new longitudinal study that focuses on the development of self-regulation to examine whether it is a sustainable hypothesis to explain the high levels of physical aggression of small number of children over time. In a first study, we identified trajectories of mother-rated physical aggression between ages 17, 30, and 42 months that were predicted by pre-birth family characteristics such as parental history of antisocial behavior, young motherhood, maternal smoking during pregnancy, low parental schooling, low income, and age 5 months characteristics such as parental coerciveness and family dysfunction (Tremblay et al., in press), essentially the same predictors for violent delinquency in the older children cohorts (Nagin & Tremblay, 2001). At ages 30, 42, and 60 months we conducted home visits where we administered a number of executive function tasks that we later put in relation with trajectories of physical aggression and hyperactivity (Séguin, Jacques, Zelazo, & Nagin, 2002). We were initially surprised to see that there were more impaired abilities associated

with hyperactivity than with physical aggression. This was opposite to what we found when the history has been documented for a longer period of time. However, we noted that those children who will really show difficulties in self-regulation of physical aggression were not yet clearly identified. On the basis of the international samples data of Broidy et al. (2003), we would expect that group to represent about 5% of all children in the sample. Our current chronic elevated group contains about 13% of children, many of whom will probably desist from the high level trajectory as they enter school. Although these results are preliminary, they already provide new insights into this complex developmental process.

There are actually a number of cross sectional and longitudinal studies that suggest that impairments cumulate over development, an interesting concept for the improvement of prevention strategies. For example, in the work of Blair and colleagues, although both OFC and amygdala function appear to be affected in adult psychopaths, only amygdala function seems to be impaired in children with psychopathic tendencies (Blair, Colledge, Murray, & Mitchell, 2001); Psychopathic adults fail to learn risk avoidance compared to psychopathic children. Mitchell et al. (2002) suggested a developmental hypothesis in which problems associated with OFC function may develop later as a result of poor amygdala function. They speculated that a reduction of afferent inputs to the OFC might, over time, have a negative impact on the responsiveness of the OFC and reduce the likelihood of risk avoidance (Mitchell et al., 2002). Similarly, Roussy and Toupin (2000) found intact odor recognition in adolescent psychopaths, although odor recognition was impaired in adult psychopaths (Lapierre et al., 1995). Odor recognition is also mediated by the OFC (Jones-Gotman & Zatorre, 1988). As Mitchell et al. (2002) suggest, the OFC in psychopathy may be more impaired in adulthood than in adolescence. A developmental perspective could thus offer a rich explanation.

Other studies also fail to find early differences in neurocognitive function of antisocial and non-antisocial children, although these tend to manifest themselves at later developmental stages. For example, Aguilar, Sroufe, Egeland, and Carlson (2000) failed to find neurocognitive differences between early onset and adolescent limited trajectories in early childhood, but were able to detect differences in later childhood. An alternative explanation is that the measurement of early neurocognitive function may not pick up mild problems which, as Blair et al. suggested, may compound other abilities over time. Also to be considered is the problem of measurement of the same neurocognitive abilities across development.

Nonetheless, these observations are fascinating because they will guide future studies of the developmental processes of frontal lobe maturation. Such studies will become a research priority (Blair, 2002). Studies must also take into account developmental history and processes. These may appear to be more complex than thought.

11. Conclusion

This review suggests that a frontal metaphor for studying antisocial disorders remains a useful one. However, a focus on primary deficits from a broadened neuroscience perspective will certainly help understand antisocial phenomena further. Nonetheless, there exist

important problems of heterogeneity and inconsistencies in measurement, whether the phenomena are approached from a neuroscience point of view (Bechara, 2002) or from a behavioral point of view (Tremblay, 2000). From a neuroscience point of view, we also note that although OFC lesions seem to be associated with variations in antisocial problems, they are rarely associated with physical violence. However, we have noted that problems of motor control such as those evidenced mainly in physical aggression have been associated with poor dorsolateral frontal lobe function; although patients with dorsolateral frontal lesions are not necessarily physically violent. Dorsolateral frontal lobe problems impair cognitive processing, mainly the working memory component of the executive function. And it may be the case that a child who has failed to learn to regulate early aggression will be more likely to be physically aggressive if such on-line problem-solving processes are impaired. Further, the work on psychopathy has emphasized emotional processing and attributes a key role to the amygdala. And a child who fails to recognize fearfulness or sadness in others is unlikely to use this information to modulate ongoing behavior. These structures regulating behavior, cognition, and emotion may be specifically implicated in antisocial problems and violence, or may be part of a complex circuit.

From a behavioral point of view, not only are antisocial phenomena varied, but the methods to study them often lack comparability. Thus the magnitude of this heterogeneity problem cannot be ascertained adequately because the overlap between methods is often poorly understood. To begin with, the constructs of psychopathy in adult and children are not necessarily isomorphic. When these are extended to acquired sociopathy, other differences emerge. Similarly, we have identified problems in the various other antisocial and externalizing nomenclatures. For example, although the physical aggression of adults may be found in toddlers, most aggressive toddlers will not become aggressive adolescents or adults. We also propose a focus on key behavioral symptoms, such as physical aggression, opposition, and hyperactivity as a complement to the broadband categories of CD and ADHD. From a legal point of view this would be translated by requesting at least clear distinctions between violent and non-violent offenders and crimes against a person or against property. Drug offences could be identified separately as well. Finally, as we improve our understanding of risk factors for antisocial behavior, we would be well advised to begin charting the development of such problems from pregnancy onwards. This will require foresight, long-term commitment, and considerable collaboration and sharing of expertise to cover the various and complex facets of these problems. Nonetheless, considerable advances have been achieved in the past 10 years since Moffitt’s critical reviews of the neuropsychology of conduct disorder (1993) and delinquency (1990b). The significant developments in the neurosciences of social behavior, cognition, and emotion have certainly contributed greatly to these exciting achievements.

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