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The frontal lobe and aggression

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Abstract

Frontal lesions often lead to psychosocial problems. It is not surprising that frontal lobe dysfunctions have been proposed to underlie antisocial behaviour in individuals without apparent lesions. However, physical aggression and violence have never been systematically related to acquired lesions. Whereas, traditional neuropsychological testing identifies problems in cognitive and emotional information processing, recent brain-imaging studies have revealed both the frontal structural and functional underpinnings of antisocial behaviour. Careful characterization of antisocial behaviour subtypes seems to indicate that cognitive-neuropsychological function is systematically poor in physical aggression and hyperactivity. Recent refinements point to biological and genetic moderators of that association.

Keywords

Neuropsychology; Aggression; Violence; Frontal lobe; Development

Back in the early nineteenth century, Phineas Gage, a reportedly mild mannered man, suffered severe but not fatal injuries to his frontal lobes during a work-related accident (see Harlow, 1993). However, after a “miraculous” recovery, his acquaintances felt he was a different person. Gage was now described as irritable, short-tempered, and obnoxious. He experienced difficulties with responsibilities, and could no longer hold down a job or provide for himself. Since that fateful accident, animal studies (Halász, Toth, Kallo, Liposits, & Haller, 2006) and several other human case studies of similar lesions have been carefully documented and provide support for a frontal-lobe hypothesis of emotional and behavioural regulation. For example, in one study of US Vietnam war veterans, those who suffered ventromedial frontal lobe injuries were shown to have higher aggressive and violent “attitudes” than a group of normal controls and a group that evidenced lesions in other brain areas (Grafman et al., 1996). Some suggest that the primary deficit following such frontal lobe lesions lies in self-reflective awareness (Stuss, Gow, & Hetherington, 1992), and perspective taking (Stuss, Gallup, & Alexander, 2001), though a broader set of abilities, such as the ability to organize complex behaviour, attention and emotional regulation are deeply affected by frontal lesions (Alexander & Stuss, 2006). These observations of individuals with verifiable lesions suggested the application of the frontal-lobe hypothesis to account for antisocial or violent behaviour in individuals who do not have obvious brain lesions. This

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paper will examine that hypothesis as it applies to aggression and violence. We will begin with an overview of neuropsychological performance as measured by traditional cognitive and information-processing tests, some of these extending to emotional processing. Then we will review key relevant structural and functional brain-imaging studies.

TRADITIONAL NEUROPSYCHOLOGICAL APPROACHES TO ANTISOCIAL BEHAVIOUR AND PHYSICAL AGGRESSION

Historically, Moffitt has reviewed studies that bear on the neuropsychological test performance of physically aggressive individuals in the context of critical reviews of the neuropsychology of delinquency (Moffitt, 1990) and of conduct disorder (Moffitt, 1993; see also Pennington & Bennetto, 1993; Teichner & Golden, 2000). This was preceded by another relevant review by Kandel and Freed (1989), which focused on antisocial behaviour, and one by Miller (1987) that focused on psychopathy. All were later followed by a review of frontal lobe involvement in aggressive behaviour that included a review of animal models (Giancola, 1995). These reviews highlighted several methodological and conceptual issues including the importance of extending inquiries beyond measurements of intelligence by using a broader neuropsychological approach. Moffitt (1990), for example, had outlined deficits in three specific areas: language abilities, executive function, and cerebral dominance. Language abilities refer mainly to those verbal skills involved in communication. Because the verbal centres are typically lateralized to the left hemisphere in most individuals, a hypothesis for poor left-brain function has been circulating in the literature. Thus, this hypothesis overlaps with a cerebral dominance hypothesis. The third concept, executive function, refers to the self-regulation of thought and action and emphasizes problem solving (Zelazo, Carter, Reznick, & Frye, 1997). Related processes are the control of inhibition and working memory, as well as language and general memory abilities. The metaphor of the executor, the one who accomplishes an action, and that of the executive, the one who identifies problems, sets goals, plans, anticipates consequences, directs, and monitors action, are most relevant to this complex concept. There is strong evidence, at least traditionally, for the neuroanatomical localization of the executive function to be largely, but not exclusively, in the frontal lobes. The bulk of research since the earlier reviews of antisocial behaviour were published focused largely on the concept of executive function as an important aspect of a frontal-lobe hypothesis. Although the executive function is influenced by both rational (“cool”) and emotional (“hot”) processes, traditional neuropsychological approaches have emphasized the more cold rational abilities, but more recent approaches have broadened the scope of this research work to include the more hot emotional levels of processing (Séguin & Zelazo, 2005).

Since the earlier reviews, one review in particular focused exclusively on traditional tests of executive function (Morgan & Lilienfeld, 2000). That meta-analytic review attempted to address some of the shortcomings of earlier studies by examining several subcategories of antisocial problems such as conduct disorder (CD), criminality, psychopathy, and antisocial personality disorder instead of using global scales of delinquency, criminality, or antisocial behaviour. This was followed by the development of a theoretical model of prefrontal function in antisocial behaviour (Raine, 2002). More recently, we have reviewed the role of

the orbitofrontal cortex in antisocial behaviour (Séguin, 2004), the role of executive function in early physical aggression (Séguin & Zelazo, 2005), and a comprehensive review of the neuropsychology of violence including an in-depth review of methodological issues (Séguin, Sylvers, & Lilienfeld, 2007b).

The neuropsychology of physical aggression: A specific research agenda

It is in the wake of the earlier reviews that we began our neuropsychological study of physical aggression. Physical aggression is perhaps the most feared of antisocial behaviours and may have its own unique etiological process and correlates. Because the above-cited reviews focused on antisocial behaviour, conduct disorder, and delinquency, it was not clear if any of these dimensions outlined by those reviews were relevant to physical aggression.

Methodological considerations—The next series of papers reviewed is based on a core methodology, which is presented below. In order to examine these questions, we identified pre-adolescent boys whose history of physical aggression since kindergarten (ages 6, 10, 11, and 12 years) had been well delineated (Séguin, Pihl, Harden, Tremblay, & Boulerice, 1995). At each age, teachers rated an initial sample of 1037 young boys from socially disadvantaged neighbourhoods on the following items: (1) “fights with other children”; (2) “kicks, bites and hits other children”; and (3) “bullies or intimidates other children”. For this first neuropsychological study, we invited a subset of these boys to our laboratory on two occasions, at age 13 ($N = 203$) and then at age 14 ($N = 177$). These boys represented three patterns of physical aggression over time defined on an a priori basis: Non-aggressive boys (never rated highly aggressive); Unstable aggressive boys (rated highly aggressive for one or two years); and Stable aggressive boys (rated highly aggressive for three or four years). The proportions of these boys who came to the laboratory in each of these groups were roughly equal. During these visits, the boys completed several tasks including cognitive-neuropsychological assessments. We carefully selected a series of neuropsychological tests that had been validated in the neuropsychological literature. Fourteen test scores were grouped into four factors. A verbal learning factor included letter and categorical fluency measures (Lezak, 1983; Lezak, Howieson, & Loring, 2004) as well as Wechsler Memory Scales digit span and paired associates (Wechsler, 1987). A spatial learning factor included scores from a task developed by Smith and Milner (1981, 1989). A cerebral dominance factor comprised scores from a Dichhaptic Lateralization task (Witelson, 1974, 1976) that consisted of using both hands to identify small shapes that were out of sight, and, a few seconds later, recognizing them visually among a series of correct and incorrect choices. Finally, an executive function factor comprised a strategic problem-solving task (Becker, Butters, Rivoira, & Miliotis, 1986), a number-randomization task (Petrides, Alivisatos, Meyer, & Evans, 1993b), the concrete and abstract versions of the self-ordered pointing task (Milner, Petrides, & Smith, 1985; Petrides, Alivisatos, Evans, & Meyer, 1993a), as well as the non-spatial conditional-association task (Petrides, 1990; Petrides et al., 1993a). These latter tasks require the effortful and “on line” manipulation of information as well as inductive or deductive reasoning, though a common characteristic of these tasks is their reliance on working memory. The last three of these tasks were validated dorsolateral frontal lobe tests. Because our focus was to test an executive function (frontal lobe) hypothesis, we entered all non-executive factors before executive function in our analysis. This is important

because there are non-executive abilities, which may rely less on the frontal lobes, and which may be necessary for executive function. Results showed specificity to executive function deficits, i.e., that executive function was poorer in both physically aggressive groups compared to non-aggressive boys over and above the effects of all other domains.

Taking hyperactivity and IQ into account—Shortly after publishing these results, an important review of the role of executive function in developmental psychopathology was published (Pennington & Ozonoff, 1996). This review was important because it supported the hypothesis that poor executive function was specific to attention-deficit hyperactivity disorder (ADHD), without comorbid psychopathology, and concluded that the evidence for an association between executive function and CD (without comorbid ADHD) was weak. The authors noted one possible exception in reviewing our earlier study (see Séguin & Zelazo, 1995), which focused on physical aggression instead of CD, one component of CD that is neither necessary nor sufficient to attribute a diagnosis of CD. They accurately noted, however, that because we had not controlled for ADHD, the question of specificity of executive function problems to CD without ADHD was still open, although again, our focus was not CD but physical aggression. Further, we could not make a clear statement about the advantages of our neuropsychological assessment over a more conventional assessment of IQ. In order to address those two issues, we followed the same boys for two years, during which time we administered two subtests of the Wechsler Intelligence Scale for Children – Revised (Wechsler, 1974), Vocabulary and Block Design, which correlate at more than .90 with the full scale IQ (Sattler, 1988), and an additional working memory task, the Spatial Conditional Association Task (Petrides, 1985, 1997). We also obtained an assessment of ADHD in adolescence using DSM-III-R criteria (American Psychiatric Association, 1987), with a French adaptation of the Diagnostic and Interview Schedule (DISC) – 2.25 using child (-C) and parent (-P) forms (Breton et al., 1999). We re-ran our initial analyses with a subset of verbal learning factor abilities (i.e., those conceptually related to short-term memory abilities necessary for working memory), and with a subset of executive function abilities related to working memory that reflected mid- and posterior dorsolateral frontal lobe function (i.e., respectively, subjective ordering—number randomization and self-ordered pointing—and spatial and non-spatial conditional association learning). Results showed poorer IQ in the physically aggressive groups, and that ADHD was present almost exclusively in aggressive groups (Séguin, Boulerice, Harden, Tremblay, & Pihl, 1999). Despite these conservative control measures, working memory task performance remained poorer in physically aggressive groups and was not significantly related to ADHD.

We suggest that we were able to support our hypothesis because we had a clear assessment of physical aggression, whereas most studies of executive function and antisocial conduct reviewed by Pennington and Ozonoff (1996) may or may not have had physically aggressive participants in their groups. This interpretation is also supported by a concurrent study that showed that only CD females who had been physically aggressive showed impairment in executive function after controlling for ADHD (Giancola, Mezzich, & Tarter, 1998). An alternative or complementary explanation is that the difference between physically aggressive and ADHD individuals may be better formulated in terms of a profile of executive function abilities. We focused on measures of working memory for theoretical

reasons, based on the work of Milner and Petrides (1984), and independently from the main currents in the literature on the neuropsychology of antisocial behaviour—although these measures were becoming better known in the antisocial-behaviour literature (Kandel & Freed, 1989). Therefore, our battery remained limited in terms of capturing the entire construct of executive function, but was strong in terms of the assessment of dorsolateral frontal lobe function and working memory.

Interestingly, it was thought that the executive function deficits observed in ADHD do not prominently affect working memory (Pennington, 1997) and our results were consistent with that idea. Instead, ADHD children, more particularly the hyperactive and impulsive subtypes, would show robust weaknesses in inhibition and planning (Pennington, 1997). However, working memory was a central element of a later proposed theory (Barkley, 1997). This illustrates the confusion that can result when referring to a construct such as “executive function” without specifying what that means. For example, several studies have failed to find an unequivocal role for executive function in CD/physical aggression or ADHD/hyperactivity (Pennington & Ozonoff, 1996) or in antisocial behaviour (Morgan & Lilienfeld, 2000) in part because of this confusion, in part due to a lack of rigorous measurement of the “other” behavioural domain. This methodological and conceptual problem had already been identified (Moffitt, Lynam, & Silva, 1994). The prediction from this line of reasoning is that early physical aggression *and* hyperactivity should be associated with the poorest neuropsychological test performance. These in turn may be associated with early onset and chronicity. We test those hypotheses further below. Nonetheless, even neuropsychological studies of ADHD that attempted to control for CD (see, e.g., Nigg, Hinshaw, Carte, & Treuting, 1998) unfortunately failed to take into account subtypes of ADHD or CD, and failed to describe their samples in terms of hyperactivity-impulsivity or physical aggression. Although methodological hurdles in this field have been reviewed recently (Nigg, 2005), the absence of methodological control for a history of theoretically relevant comorbid symptom clusters was also clearly identified as a limitation by Raine, Buchsbaum, and LaCasse (1997) in their brain-imaging studies of murderers reviewed below. Unless such controls are applied prospectively (or at least retrospectively with validation from a second observer such as a school teacher), claims of specificity have only weak empirical value.

In order to clarify these issues, we have reassessed the community sample of boys we had been following since kindergarten when they were age 20 years ($N = 303$). We innovated in two significant ways. First, instead of selecting boys on the sole basis of their history of physical aggression, we selected them jointly on this and their history of hyperactivity. We used the trajectories that had been computed by Nagin and Tremblay (1999). In contrast to our previous a priori method of grouping children as a function of their behavioural history, trajectories are empirically based. This method identifies groups of individuals whose developmental trajectories do not necessarily follow the average trend of decrease in physical aggression or hyperactivity levels across time. Second, we noted that past studies that used one secondary behaviour to control for a primary behaviour of interest revealed information only on the unique neuropsychological variance with that primary behaviour. It provided little information on the neuropsychological profile of those children with greater comorbidity and did not allow for studying the unique variance associated with the

secondary behaviour. Although some studies had previously considered primary and secondary behaviours simultaneously, they did so in a single-factor model, which precluded accurate tests for additive and synergistic effects (Waschbusch, 2002). Using a factorial model instead, we were able to identify that the physical aggression and hyperactivity combined in an additive fashion with several neuropsychological and IQ tests, though some were only sensitive to a history of physical aggression (Séguin, Nagin, Assaad, & Tremblay, 2004).

The joint development of neuropsychological function and physical aggression—We have now changed our research focus in order to understand the factors underlying this joint development of neuropsychological function and physical aggression. Four recent findings are noteworthy. First, we note that the relationship that we and others find between physical aggression/hyperactivity problems and neuropsychological function can be identified as early as the preschool years (Séguin & Zelazo, 2005). Second, though maternal prenatal smoking does not appear to be related to cognitive function in preschoolers once we control for maternal education (Huijbregts et al., 2006), maternal prenatal smoking predicts the joint development of physical aggression and hyperactivity in preschoolers (Huijbregts, Séguin, Zoccolillo, Boivin, & Tremblay, 2007). Third, the overall negative correlation between neuropsychological function and externalizing behaviour appears to be mediated by the dopamine receptor gene DRD4 (DeYoung et al., 2006). A variant of this gene, the one with the 7th repeat allele, which is found in approximately 15% of the Caucasian population, seems to impair the functioning of the D4 receptor. Blockage of the D4 receptor is also known to attenuate the cognitive deficits observed in schizophrenia. Otherwise, dopamine activation is related to impulsive and other externalizing behaviour problems. Thus, the negative correlation was only found in men without the genetic variant. There was no correlation between IQ and externalizing behaviour problems in those who had the 7th repeat allele. This important finding was replicated in three samples including a sample of ADHD adults, a clinical sample of children referred for aggressive problems, and our community sample described above (DeYoung et al., 2006). Fourth, as raised earlier, there were questions regarding the validity of studying the neuropsychology of CD as a whole instead of focusing on key symptom groups such as those involving violence and theft. We addressed this issue with a sample drawn from Rutgers University in the United States in which there was no correlation between neuropsychological function and delinquency trajectories (White, Bates, & Buyske, 2001). However, when we broke down delinquency into physical aggression and theft, we first found that the trajectories were not identical and, second, that the typical negative correlation of neuropsychological function was with physical aggression only, whereas the correlation was actually reversed and positive for theft (Barker et al., 2007). This essentially suggests that all future studies of CD now need to consider a symptom approach if we are to make significant progress in understanding the etiology of this important disorder.

NEUROLOGICAL PROBLEMS ASSOCIATED WITH ANTISOCIAL BEHAVIOUR THAT ARE NOT SENSITIVE TO TRADITIONAL NEUROPSYCHOLOGICAL TESTING OR PHYSICAL AGGRESSION

Although we just reviewed the literature on the neuropsychology of physical aggression, the cases reviewed in the introduction to this paper, and from which a frontal hypothesis of aggression was derived, did not appear (1) to show impairments on the traditional neuropsychological tests just reviewed, or (2) to systematically show signs of physical aggression.

Accounting for emotional processing deficits in antisocial behaviour

Following Phineas Gage's accident, intelligence, new learning, and memory, assessed with neuropsychological testing procedures of the day, were reportedly all intact. In reconstructing the neuroanatomical features of this case with the help of Gage's skull and modern imaging techniques, Hannah Damasio and her colleagues (1994) were able to determine that the lesions were mainly located in the orbitofrontal lobe and the ventromedial frontal lobe, although there is some degree of controversy about this finer point (Ratiu, Talos, Haker, Lieberman, & Everett, 2004). In contrast, the "cool" executive function tests we reviewed above were particularly sensitive to the dorsolateral areas of the frontal lobes. If this reconstruction is exact, it would lend support to a hypothesis that Antonio and Hannah Damasio and their colleagues have put forward regarding the role of these brain areas in rational decision making and the processing of emotions (Damasio, 1996; Damasio, Tranel, & Damasio, 1991). The "somatic markers hypothesis" suggests that ventromedial frontal lobe lesions impair the capacity to consider emotions when making a decision that involves a significant degree of uncertainty. This impairment is characterized by relatively greater sensitivity to rewards than to punishment cues, an inability to learn from previous mistakes, and impaired emotional reactions. Behaviourally, this would explain the disadvantageous moral, social, and financial consequences that plague the lives of individuals with such a deficit. Because of this, the resulting syndrome was called "acquired sociopathy" (Damasio, 2000; Damasio, Tranel, & Damasio, 1990; Naqvi, Shiv, & Bechara, 2006; Saver & Damasio, 1991), or "pseudopsychopathic syndrome" (Moffitt, 1990; Stuss & Benson, 1984). A similar case with left unilateral orbitofrontal damage in adulthood was described as "acquired antisocial personality disorder" (Meyers, Berman, Scheibel, & Hayman, 1992). In this latter case, performance on cognitive-neuropsychological tests was also unimpaired despite obvious personality changes and an inability to maintain an occupation. However, more recent evidence does not dispute the observed behaviour but suggests a slightly different interpretation for the role of the brain structures underlying these neurobehavioural sequelae (Manes et al., 2002; Séguin, 2004). In sum, emotional "hot" information is necessary to make adaptive rational "cool" decisions.

Nonetheless, at an information-processing level, individuals with these types of lesions typically show poor performance on cognitive tasks designed to assess decision making under conditions of reward and punishment, i.e., when "hot" executive function is required (Bechara, Damasio, Damasio, & Anderson, 1994; Bechara, Tranel, & Damasio, 2000;

Séguin, Arseneault, & Tremblay, 2007a). One task designed to assess this ability consists of four decks of cards that each contain a predetermined sequence of gains and losses (Naqvi et al., 2006; Yechiam, Busemeyer, Stout, & Bechara, 2005; a version for children has also been developed by Kerr & Zelazo, 2004). Briefly, two decks are disadvantageous and two are advantageous. The disadvantageous decks provide high gain but even higher cost, while the advantageous decks provide low reward, but even lower costs. In this manner, it is only possible to make gains over 100 trials by selecting the advantageous decks. Authors claim that the task is thus designed to be an analogue of real-life decision-making situations. The individual plays cards from any deck but is typically instructed that "some decks are better than others". Thus, instructions for this task, unlike many tasks that require the figuring out of an underlying rule in an inductive-reasoning fashion—the Wisconsin Card Sort Task (Anderson, Damasio, Jones, & Tranel, 1991), Conditional Association Tasks (Petrides, 1985, 1997), other card-playing tasks (Séguin, Arseneault, Boulerice, Harden, & Tremblay, 2002; Séguin et al., 2007a), and some Go/No-go discrimination tasks (Arnett, Howland, Smith, & Newman, 1993; Yechiam et al., 2006) are some examples—state the rule explicitly but fall short of indicating to which deck(s) the rule applies. Recent advances have decomposed performance on this task into three key components that may be useful to untangle cognitive ("cool") from motivation ("hot") effects (Yechiam et al., 2005). The interesting findings from these case studies have prompted more studies in individuals who show impulsivity (Ramaekers & Kuypers, 2006), antisocial behaviour (Ernst et al., 2003; Lösel & Schmucker, 2004; Mitchell, Colledge, Leonard, & Blair, 2002), alcohol (Dom, De Wilde, Hulstijn, van den Brink, & Sabbe, 2006) and drug addiction (Bechara & Martin, 2004) or a tendency to gamble (Goudriaan, Oosterlaan, de Beurs, & van den Brink, 2005) to support the generalizability of this component of the somatic markers hypothesis. It is not yet fully clear if the main impairment across these behavioural problems is one in which decisions are made without emotional input or if highly charged emotional situations impair otherwise perfectly normal problem-solving skills (Séguin et al., 2007a). We have indeed shown that neuroticism, an index of emotional lability, selectively increased risk for dysregulation of problem solving in boys with an unstable history of physical aggression compared to boys with a stable history of physical aggression and non-aggressive boys, even after control for short-term and working memory and hyperactivity (Séguin et al., 2002). Otherwise, cognitive-neuropsychological abilities between these two groups did not differ (Séguin et al., 1995, 1999). Thus, there may be personality and environmental characteristics that interact to impair decision making. Such a hypothesis has been invoked to explain various forms of psychopathy (Sugrue, Corrado, & Newsome, 2004).

Lesions and physical aggression

The mostly adult neurological case studies listed above, provide valuable natural experiments that show how the brain may be involved in antisocial behaviour. However, frontal lesions do not systematically lead to physical aggression or violence. At a developmental level, only a few case studies of early prefrontal injury and behaviour have been published (Benton, 1991; Eslinger, Flaherty-Craig, & Benton, 2004). A number of these involve early brain lesions in the target areas we have been discussing and lead to chronic adaptation problems that resemble psychopathy (Anderson, Bechara, Damasio, Tranel, & Damasio, 1999; Eslinger & Grattan, 1991) but, again, may not necessarily lead to

physical aggression (Eslinger et al., 2004) except for one study where bilateral frontal damage early in a boy's life was associated with assault and developmental immaturity, although IQ was normal, and general memory was intact (Price, Daffner, Stowe, & Mesulam, 1990). One of the reasons for that state of affairs is that most of the cases reviewed involved acquired lesions. Thus, the individuals may have developed in an otherwise "normal" background. Even in adults, a similar case to that of Phineas Gage was able to lead a moderately adaptive life when provided with a strong and coherent environmental structure (Mataro et al., 2001). Therefore, developmental background may be an important moderator of the risk for physical aggression.

BRAIN IMAGING INSIGHTS INTO THE NEUROPSYCHOLOGY OF ANTISOCIAL BEHAVIOUR AND PHYSICAL AGGRESSION

Functional imaging—Although orbitofrontal and ventromedial lesions do not appear to lead to violence, there is evidence that the ventromedial and orbital frontal lobes may be involved in the regulation of physical aggression as well. Pietrini, Guazzelli, Basso, Jaffe, and Grafman (2000) recorded brain activity in 15 "normal" volunteers with good mental imagery abilities while they imagined four different scenarios. All scenarios involved the participant, their mother, and two male strangers taking an elevator ride. The ride was uneventful in the neutral condition. However, the two men assault the mother in the three aggressive scenarios. Thus, the context involved a high level of provocation that heightened the likelihood of reactive aggression. The aggressive scenarios varied as a function of the restraint that was imposed on the participant. In the first aggressive scenario, the participant observed and did not attempt to intervene. In the second aggressive scenario, the participant attempted to intervene but was restrained by one of the men. In the third aggressive scenario, the participant was unrestrained and was instructed to "seriously injure or kill" the assailants (Pietrini et al., 2000, p. 1773). Compared to the neutral condition, 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. In the unrestrained condition, there was also visual activation, which the authors speculated may have been related to motor imagery, and cerebellar activation, which may have been due to inhibition of motor programs or to emotional processing. This supports a longstanding element of the frontal hypothesis in that it is the ventromedial frontal cortex that played an inhibitory role, and the less the participant was restrained in the fantasy of defensive aggression, the less suppression occurred. However, the Pietrini et al. (2000) study shows that processing observed in individuals who suffered some types of brain lesions giving rise to such a syndrome can be extended to *normal/non-lesioned/non-aggressive* individuals and that the ventromedial frontal cortex may be involved in the self-regulation of, at least, some forms of physical aggression. The authors further speculated that the self-regulation processes of the orbitofrontal lobe are achieved either by suppression of inappropriate action in response to provocation or by activation of alternative behaviour. Finally, and in accord with other recent studies (Blair & Cipolotti, 2000; Blair, Morris, Frith, Perrett, & Dolan, 2000), the authors concluded that the major function of this brain region may be about awareness and processing of emotions and control of emotionally driven behaviour. Because of this, poor orbitofrontal frontal lobe functions are not exclusively related to antisocial behaviour against

others, but may also be involved in other maladaptive behaviour patterns such as those associated with the somatic markers hypothesis.

Another set of studies may speak more directly to an application of the frontal-lobe hypothesis to physical aggression. Raine and colleagues (1994) conducted a series of studies on a heterogeneous group of suspected murderers pleading not guilty by reason of insanity (SMPNGRI) and found reduced activity circumscribed to the anterior left prefrontal cortex while tested on a Continuous Performance Task (CPT), a measure of sustained attention. The authors noted a tendency for individuals who had committed impulsive murders to show lower prefrontal function than individuals who had committed planned murders. Raine, Phil, Stoddard, Bihrle, and Buchsbaum (1998) further compared the SMPNGRI who had a history of psychosocial deprivation (abuse or neglect) to those without such a history. They observed prefrontal deficits while using the CPT that were more severe in non-psychosocially deprived murderers, which provides strong support for a biological *vulnerability* for violence in that group: The other group showing a more developmentally adverse background that could be at the origin of their antisocial behaviour. In that series of studies, SMPNGRI did not differ from control groups on the CPT, which provides a control for test motivation. The authors speculated that other brain areas not usually utilized for this task might have compensated for the lack of left frontal lobe function (Raine et al., 1994). One extension of those studies indicated that CPT performance actually involves more than the frontal cortex and includes other cortical and subcortical areas (Raine et al., 1997). Although this supports the concept that the frontal lobe may be only one component of a network involved in the regulation of sustained attention, that network of structures differed significantly across groups (Raine et al., 1997). Thus, in addition to possibly identifying a dysfunctional neural circuit of emotion regulation that underlies some forms of violence (Amen, Stubblefield, Carmichael, & Thisted, 1996; Davidson, Putnam, & Larson, 2000), one very important implication of this research is that violent individuals may perform several functions as well as non-violent individuals but by using alternate neural circuits to achieve the same results. In other words, between-groups traditional neuropsychological test scores would not differ quantitatively, but the processes underlying such performance would differ qualitatively.

Structural imaging—The physiological changes documented by imaging techniques may also have morphological parallels. Raine, Lencz, Bihrle, LaCasse, and Colletti (2000) also showed an average 11% reduction in frontal cortex grey matter in Antisocial Personality Disorder as well as corpus callosum structural abnormalities in psychopathic and antisocial individuals (Raine et al., 2003). Further, this group of researchers has also shown poorer executive function (Ishikawa, Raine, Lencz, Bihrle, & LaCasse, 2001), hippocampal asymmetry (Raine et al., 2004) and prefrontal reduction in grey matter (Yang et al., 2005) in those psychopaths that are unsuccessful. The study of such morphological characteristics in several disorders of self-regulation has increased significantly in recent years and, like functional brain-imaging studies, also encompasses cortical as well as subcortical structures (Driessen et al., 2000; Eliez & Reiss, 2000).

Summary

In sum, studies of the orbital frontal lobe and ventromedial frontal lobe have implicated these structures in antisocial behaviour and severe violence, but they have not established an unambiguous relationship with physical aggression. Nonetheless, studies of SMPNGRI reveal a level of complexity in brain function of violent individuals that extends beyond the frontal lobe. Although exciting, these results must be welcomed with a cautious enthusiasm. Care must be exerted (a) in generalizing findings from one group of individuals who may also show either violent or antisocial behaviour to another, (b) in drawing any cause – effect conclusion (e.g., that biology alone is driving these behaviours), and (c) in using brain-activity patterns or neuropsychological test-performance profiles as diagnostic tools (Beckman, 2004; Eastman & Campbell, 2006; Raine et al., 1997). Although the state of current brain-imaging studies supports hypotheses of brain differences between psychopathologies of interest, they need to be complemented by comprehensive assessments of the abilities involved. Functional-imaging studies such as those of the SMPNGRI are admittedly limited because the brain differences are typically observed during performance of one single task (Raine et al., 1997). However, the fact that SMPNGRI and controls did not differ on that task but did differ in terms of the underlying brain activity involved in performance of that task is an important feature. This suggests that, beyond differences in performance on varied tests, performance on tests where there are no score differences between groups may also show differences in the brain mechanisms involved. Further, some underlying pathology may be missed with brain-imaging techniques but identified with EEG, for example (Gatzke-Kopp, Raine, Buchsbaum, & LaCasse, 2001). This adds a level of complexity that must be incorporated in accounts of the neuropsychology of aggression.

CONCLUSIONS AND RESEARCH AGENDA

This review has highlighted several key factors that enable us to appreciate the role of the frontal lobe in aggression and physical aggression. First, we noted that frontal lesions are likely not sufficient to cause physical aggression or violence, though they often cause severe psychosocial impairments. Second, impairments in decision making are found in many conditions associated with an antisocial lifestyle such as drug and alcohol abuse, and gambling. These seem to be subsumed by the more ventral areas of the frontal lobes and to involve impairments in the processing of emotions. The somatic markers hypothesis proposes that individuals with such lesions are deprived of key emotional information that impairs their ability to make adaptive decisions. A complementary proposal is that individuals who have particular emotional sensitivities may see their otherwise intact problem-solving abilities impaired, if not severely biased, under specific situations, such as those involving cues for punishment or reward. However, the emotional regulation problems here may not be based in the frontal lobes, such as the somatic markers hypothesis suggest. They may involve more attentional processes and automatic biases in information processing. Although these complementary proposals are relevant to antisocial behaviour problems and involve “hot” decision making, none seem to be specific to physical aggression or violence.

Third, our own work shows that when we specify physical aggression as a necessary symptom, we do find clear neuropsychological impairments in general and in executive function in particular across developmental stages. Here we also refer to impairments in the "cooler" more rational function associated with the dorsolateral frontal lobe. This finding applied also to hyperactivity and it is individuals with both behaviour problems who were the most impaired. In contrast, when physical aggression is disentangled from other delinquent or antisocial behaviours, such as theft, its negative association with neuropsychological function also appears to be much stronger because of statistical suppression. Therefore, some behaviours are in an additive relation to physical aggression, whereas others are in a "subtractive" relation when it comes to neuropsychological function. Fourth, several studies have helped identify key additional moderating factors of that association. These include genetics of the dopaminergic system, and developmental background, whether it is biological or psychosocial. Fifth, at a conceptual level, brain-imaging studies show that although some neuropsychological abilities may appear to be unimpaired in some antisocial individuals, the cerebral networks underlying these abilities may be qualitatively different from those of non-antisocial individuals.

Together, these findings should help guide further research to uncover the combination of characteristics that increase the propensity for physical aggression and violence. Future studies would benefit by considering multi-method approaches to assessment of behaviour and frontal function as those reviewed above. The many prospective developmental studies that are ongoing will be strong assets in this endeavour. Early prevention studies, beginning during pregnancy, would bring experimental evidence to bear on the essentially correlational literature we have today. Nonetheless, as relatively very few individuals from epidemiological samples are at risk for lifetime histories of physical aggression or violence, a complement of carefully conducted clinical studies will be necessary. It will also be important to understand the violent individuals whose frontal functions appear to be intact or unrelated to their aggressive behaviour such as the individuals with the DRD4 – 7 repeat genotype, those who show both propensities to violence and theft, or those who are successful.

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