Arrested development: early prefrontal lesions impair the maturation of moral judgement

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Learning to make moral judgements based on considerations beyond self-interest is a fundamental aspect of moral development. A deficit in such learning is associated with poor socialization and criminal behaviour. The neural systems required for the acquisition and maturation of moral competency are not well understood. Here we show in a unique sample of neurological patients that focal lesions involving ventromedial prefrontal cortex, acquired during development, result in an abnormally egocentric pattern of moral judgement. In response to simple hypothetical moral scenarios, the patients were more likely than comparison participants to endorse self-interested actions that involved breaking moral rules or physically harming others in order to benefit themselves. This pattern (which we also found in subjects with psychopathy) differs from that of patients with adult-onset ventromedial prefrontal cortex lesions—the latter group showed normal rejection of egocentric rule violations. This novel contrast of patients with ventromedial prefrontal cortex lesions acquired during development versus during adulthood yields new evidence suggesting that the ventromedial prefrontal cortex is a critical neural substrate for the acquisition and maturation of moral competency that goes beyond self-interest to consider the welfare of others. Disruption to this affective neural system early in life interrupts moral development.

Keywords: prefrontal cortex; moral development; moral judgement; emotion; egocentric
Abbreviation: PFC = prefrontal cortex

Introduction

Moral rules are the normative fabric of civilized society, and learning to abide by them is crucial for adaptive functioning in a complex social environment (Crick and Dodge, 1994). Atypical moral development is associated with antisocial and criminal behaviours that are an immense burden to society (Blasi, 1980; Blair, 1995), with costs estimated at over $1 trillion annually in the USA (Anderson, 1999). Despite extensive study of moral development (Killen and Smetana, 2006), the incidence of antisocial behaviour has not been effectively reduced (Dodge et al., 2006).
A hallmark of human moral development is the maturation of moral judgements, which, as individuals develop through childhood and adolescence, come to be based less on egocentric self-interest and more on empathic concern for others and an appreciation for justice and reciprocity (Piaget, 1932; Kohlberg, 1969; Rest et al., 2000). Many social skills emerge early in life (Thompson, 2012), and some degree of pro-sociality may be exhibited earlier in life than previously thought, constituting early milestones in moral development (Hamlin et al., 2007; Fehr et al., 2008). The maturation of moral judgement, transitioning from selfish to social, has long been theorized as an essential marker of typical social and moral development (Kohlberg, 1969; Rest et al., 2000).

The neurological mechanisms underlying this fundamental aspect of moral development are unknown. Two related lines of research set the stage for the current neuropsychological study. First, while Kohlberg’s seminal work rooted moral development in abstract reasoning, current views suggest an important role for social emotions (Damasio, 1994; Haidt, 2001; Greene, 2007; Malti and Latzko, 2010). Second, the ventromedial prefrontal cortex (PFC) is a critical neural substrate for the social-emotional functions thought to be involved in moral development (Damasio et al., 1990; Beer et al., 2003; Camille et al., 2004; Decety et al., 2012; Decety and Howard, 2013). Patients with ventromedial PFC lesions acquired in adulthood exhibit abnormally utilitarian judgements about ‘high-conflict’ moral scenarios that place demands on the need to integrate social emotions into the complex reasoning process (Koenigs et al., 2007; Thomas et al., 2011), suggesting that the affective functions of the ventromedial PFC may be necessary for normal moral judgement (Damasio, 1994). Accordingly, it has been proposed that dysfunction of the ventromedial PFC (on the neural side) and impaired empathy (on the psychological side) play central roles in psychopathy, a neurodevelopmental disorder hallmark by callous, egocentric and impulsive antisocial behaviour (Kiehl, 2006; Blair, 2008).

The study of rare neurological patients with antisocial and amoral behaviour as a result of focal lesions acquired during development could reveal brain areas and processes that are critical for the acquisition and maturation of moral competency. We previously reported two cases of individuals with developmental-onset ventromedial PFC injury (Anderson et al., 1999; Eslinger et al., 2004) who exhibited amoral behaviour and a lack of empathy. Moreover, social conduct problems in the two developmental-onset ventromedial PFC patients were distinctly more severe than those typically observed in patients with adult-onset ventromedial PFC lesions, hinting that the ventromedial PFC may play a necessary role in moral development. This could be due, in turn, to impaired learning of the aversion to self-serving moral transgressions based on complex social-emotional reinforcement contingencies (e.g. punishment for selfish behaviour that is harmful to others; Bechara et al., 1997; Blair, 2007; Jones et al., 2011).

This preliminary evidence points to the idea that the ventromedial PFC may be critical for the acquisition and maturation of moral faculties, and that early dysfunction in this region may result in an immature, abnormally egocentric moral sensibility. Damage to ventromedial PFC that occurs later in life may not affect this early phase of moral development, although ventromedial PFC damage acquired at any time likely still affects the ability to integrate social-emotions (e.g. an aversion to harming others or to performing selfish actions) into reasoning about novel, complex moral situations (Koenigs et al., 2007; Thomas et al., 2011). Here, taking advantage of a unique opportunity afforded by a rare collection of neurological patients, we put this prediction to an empirical test. Specifically, we tested our primary hypothesis that patients with developmental-onset ventromedial PFC injury would exhibit more egocentric, self-serving moral judgements than adult-onset ventromedial PFC injured patients when judging low-conflict moral scenarios that pit self-interest against a moral norm (e.g. Would you lie on your taxes to save money?)—a result which would highlight a critical role for the ventromedial PFC in moral development. We contrasted the developmental-onset ventromedial PFC injured patients to comparable patients with developmental-onset brain damage outside of the ventromedial PFC (developmental brain-damaged comparison group) and neurologically healthy adults (neurologically healthy group). We also tested the hypothesis that developmental and adult-onset ventromedial PFC groups would exhibit more self-serving moral judgements relative to comparison participants when judging complex (high-conflict) moral scenarios (e.g. Would you push someone off a lifeboat to save yourself and the other passengers?), which place demands on emotion-reasoning integration.

**Materials and methods**

**Participants**

Patients were recruited from the Iowa Patient Registry. We recruited individuals with developmental-onset (at ≤16 years of age) lesions to the ventromedial PFC (n = 8; Table 1; Supplementary Table 1). For comparison, we recruited a brain-damaged comparison group (n = 9) of individuals with developmental-onset lesions outside the ventromedial PFC that did not significantly intrude on other putative emotion-processing structures (amygdala, insula). Previous data from adult-onset ventromedial PFC (n = 6) and neurologically healthy (n = 12) groups were used with permission (Koenigs et al., 2007). All participants gave written informed consent.

**Neuroanatomical analysis**

Neuroanatomical analysis was based on magnetic resonance (or CT for one developmental control patient) data obtained >3 months after lesion onset. Developmental-onset ventromedial PFC (Fig. 4) and developmental control lesions were analysed qualitatively on a case-by-case basis. Adult-onset ventromedial PFC lesions were analysed previously (Koenigs et al., 2007).

**Stimuli and task**

Participants made judgements on 50 hypothetical scenarios (which have been used extensively in previous studies; Greene et al., 2001; Koenigs et al., 2007; see Supplementary material for stimuli) on a computer. Stimuli and procedure were identical to those in Koenigs et al. (2007). After each scenario was described, a yes/no yes question about a hypothetical action was presented (‘Would you… in order to…?’).
The moral scenarios are either ‘high-conflict’ (n = 13), in which the options present competing social-emotional (personal) and utilitarian considerations (e.g. smothering a crying baby to save a group of people), or ‘low-conflict’ (n = 18), in which at least one of those conflicting considerations is absent (Koenigs et al., 2007; Thomas et al., 2011). One scenario did not fit these categories (see Supplementary material) and was not included in the analyses. The low-conflict scenarios are further subdivided into: (i) self-serving scenarios (n = 12), which probe the integrity of moral development towards non-self-serving judgements by pitting a self-serving action against a moral rule (e.g. lying to save money on taxes, killing an annoying boss); and (ii) utilitarian scenarios (n = 6), pitting a utilitarian principle against an impersonal harm (e.g. lying to save others from physical harm).

Participants with normal development of the ventromedial PFC (adult-onset ventromedial PFC, developmental brain-damaged comparison, and neurologically healthy groups) exhibited near-universal endorsement of the low-conflict self-serving actions (endorsements >95%), and near-universal endorsement of the low-conflict utilitarian actions (endorsements >89%). Because endorsement of the low-conflict self-serving actions would thus unambiguously indicate an abnormally egocentric pattern of moral judgement (i.e. clear violation of a moral norm in favour of self-interest), these scenarios provide the key test of our main study hypothesis.

As the high-conflict scenarios pit two competing moral norms against one another (e.g. the de-ontological norm against committing ‘personal’ harm versus the more utilitarian norm of maximizing the lives saved; Greene et al., 2001), there is not a response option that reflects sole self-interest (in contrast to the low-conflict self-serving scenarios). Nonetheless, to explore self-serving moral judgement in such high-conflict scenarios, we subdivided the high-conflict scenarios into those in which the proposed action secures a utilitarian outcome (high-conflict non-self-serving) or a utilitarian outcome that is also self-serving (high-conflict self-serving).

### Data analysis

Repeated-measures logistic regression was used to assess the effect of group membership on the likelihood of endorsing the proposed actions in the various scenarios. As the key test of our main study hypothesis, we predicted that the developmental-onset ventromedial PFC group would be more likely to endorse self-serving actions relative to the adult-onset ventromedial PFC group (and both comparison groups) on the low-conflict self-serving scenarios. Also, in keeping with the idea that this effect would be specific to self-serving judgements, we predicted that the developmental-onset ventromedial PFC group would be similar to the other groups on non-moral and low-conflict utilitarian scenarios.

Finally, the developmental function of the ventromedial PFC suggests that moral development will be arrested at the time of ventromedial PFC damage; i.e. damage impairs further moral development but does not abolish moral knowledge already established by the time of injury. Thus, we conducted a preliminary analysis to test the prediction that across all patients with ventromedial PFC lesions, age of onset of ventromedial PFC damage would be inversely related to self-serving moral judgement on the low-conflict scenarios (i.e. earlier onset associated with greater likelihood of self-serving moral judgement). Finally, we predicted that in the more ambiguous, high-conflict scenarios, all ventromedial PFC patients would be more likely than comparison participants to endorse self-serving actions that harm others due to a putative role for the ventromedial PFC in integrating an aversion to such self-serving actions into moral judgement.
Results

The findings supported the predictions. In the critical test of our main hypothesis, on the low-conflict self-serving scenarios (Fig. 1A) the developmental-onset ventromedial PFC group was significantly more likely to endorse the self-serving action than all other groups [neurologically healthy: odds ratio (OR) = 17.519, \( P < 0.0001 \); developmental brain-damaged comparison: OR = 13.078, \( P < 0.0001 \); adult-onset ventromedial PFC: OR = 5.638, \( P = 0.01 \)]. Importantly, and supporting our second prediction, this between-group difference was specific to low-conflict self-serving scenarios: for non-moral and low-conflict utilitarian scenarios (Fig. 2), there were no significant differences between the developmental-onset ventromedial PFC group and any other groups (non-moral: neurologically healthy, OR = 1.363, \( P = 0.053 \); developmental brain-damaged comparison, OR = 1.215, \( P = 0.25 \); adult-onset ventromedial PFC, OR = 1.10, \( P = 0.60 \); low-conflict utilitarian: neurologically healthy, OR = 0.633, \( P = 0.59 \); developmental brain-damaged comparison, OR = 0.912, \( P = 0.90 \); adult-onset ventromedial PFC group, OR = 0.509, \( P = 0.40 \)). There were no significant differences between any of the other groups on either type of low-conflict scenario (all \( P \)-values \( > 0.1 \)).

In support of the prediction that earlier damage to the ventromedial PFC would be associated with a higher likelihood of endorsing low-conflict self-serving actions, we found that ventromedial PFC patients with the earliest onset (before age 5) exhibited the greatest endorsement of such actions, a pattern that was marginally significant compared to ventromedial PFC patients with onset during school-age years (ages 8 to 17, OR = 1.49, \( P = 0.092 \)) and highly significant compared to ventromedial PFC patients with onset in adulthood (ages 30–60, OR = 6.77, \( P = 0.004 \)). Additionally, onset during school-age years resulted in greater endorsement than onset in adulthood (odds ratio = 4.55, \( P = 0.028 \)) (Fig. 1B).

We also tested a model that included a term for the interaction of ventromedial PFC damage (ventromedial PFC versus comparison participants) with high-conflict scenario type (self-
serving versus non-self-serving), which yielded a significant result (Wald = 3.93, \( P = 0.048 \)). Both comparison groups exhibited lower endorsement of scenarios with versus without self-interest (neurologically healthy, OR = 0.41, \( P = 0.01 \); developmental brain-damaged comparison, OR = 0.64, \( P = 0.029 \)), whereas the developmental-onset ventromedial PFC and adult-onset ventromedial PFC groups did not show this effect (\( P \)-values > 0.7; Fig. 3). An analysis of all high-conflict scenarios together is presented in the Supplementary material for comparison with previous studies.

**Discussion**

Understanding the neurobiology of moral development may be a key step in developing more effective treatment and prevention strategies for antisocial behaviour. The study of patients with early-onset brain injuries offers a unique source of data in this regard; such patients can reveal whether discrete brain areas are necessary for the acquisition and maturation of particular moral faculties. To date, the only available evidence of this type has been a few case reports of early-onset damage to the prefrontal cortex (Anderson et al., 1999; Eslinger et al., 2004) that suggest an association between developmental prefrontal damage and psychopathic behaviour. Here, we used a unique neurological patient sample to perform the first systematic study of moral competence after developmental prefrontal damage, and included a direct contrast between developmental-onset and adult-onset ventromedial PFC lesions that yields compelling evidence in support of the conclusion that the ventromedial PFC plays a critical role during development in acquiring basic moral sensibilities regarding the welfare of others.

The novel and important finding from our study is that patients with developmental-onset lesions to the ventromedial PFC, unlike patients in whom ventromedial PFC damage occurred during adulthood, endorsed significantly more self-serving judgements that broke moral rules or inflicted harm on others—e.g. lying on one’s taxes or killing an annoying boss. Furthermore, a preliminary analysis suggested that earlier ventromedial PFC damage, especially before the age of 5 years, resulted in a greater likelihood of self-serving moral judgements. Although the \( n \) is small, our results can be taken to suggest that as children age, they may be more likely to have advanced further in moral development and therefore become less likely to have the early socialization process impaired by ventromedial PFC dysfunction, suggesting that intact ventromedial PFC functioning could be most crucial to moral development in early childhood. In fact, this conclusion was predicted in the previous study by our group that focused on two early-onset patients (Anderson et al., 1999).

The small number of patients in our study is a limitation, although we would also underscore that our current \( n \) is the largest to our knowledge of such rare developmental neurological cases. Also, the ages of onsets for the developmental-onset ventromedial PFC patients are variable and range across different periods of development. Adding other cases to this data set will be important to corroborate the current findings and clarify possible critical developmental stages. In spite of these limitations, the evidence presented here provides important support for the idea that the
ventromedial PFC, which is a central node in the affective frontolimbic neural system, is necessary for the typical internalization of basic moral rules regarding self-interest during development (Blair 2007; Decety and Howard, 2013).

As individuals age, there is increased functional coupling between the ventromedial PFC and amygdala during the apprehension of moral stimuli (Decety et al., 2012), and dysfunction of the ventromedial PFC before moral circuitry maturation may disrupt coordinated activity within this network. We highlight two central processes in the pathways through which such frontolimbic dysfunction may disrupt moral development. First, early ventromedial PFC dysfunction may render the individual less sensitive to social scaffolding when it is present (Kochanska, 1994). An impaired ability to use emotions and feelings to guide behaviour could impede the ability to learn an aversion to self-serving actions—and thus learn right and wrong (Decety et al., 2012)—from complex social reinforcement contingencies (e.g. getting punished by peers or caregivers for self-serving behaviour and rewarded for pro-social behaviour; Damasio, 1994; Blair, 2007). In addition, environmental factors could contribute to reduced functional integrity of the ventromedial PFC (Hanson et al., 2010).

Second, in some cases early ventromedial PFC dysfunction may lead to a biology × environment interaction wherein a child with impaired social-emotional functioning is at risk for disrupted moral development when peer and caregiver interactions fail to build appropriate scaffolding for the child’s moral development (Caspì et al., 2002; Laible and Thompson, 2002; Dunn, 2006). Such children may even be less likely to elicit these scaffolding interactions because of their atypical social behaviour, further setting the table for disrupted moral development and antisocial behaviour (Sroufe, 1995). Further research will be needed to tease out how these complex pathways disrupt moral development.

Importantly, once moral norms against selfishness are learned, they appear to become standard moral knowledge (e.g. they are nearly universally agreed upon among comparison participants). Moreover, they are no longer impacted by damage to the prefrontal lobes (adult-onset ventromedial PFC patients respond typically), suggesting that affective, frontolimbic input is no longer necessary for the verbal, off-line implementation of such rules.

We should note too that the main result is not driven by lesions in the developmental-onset ventromedial PFC group that extended beyond the ventromedial PFC, or by the one developmental-onset ventromedial PFC patient with lesion onset in adolescence (likely still before full development of the prefrontal cortex; Gogtay et al., 2004; see Supplementary material for analyses).

Dysfunction of the frontolimbic system during development has been suggested as an aetiological mechanism in psychopathy (Kiehl, 2006; Blair, 2008), and this would predict that persons with psychopathy might exhibit egocentric moral judgments similar to those of developmental-onset ventromedial PFC patients. We tested this hypothesis in a reanalysis of data from a recent study that administered a similar stimulus set to participants with psychopathy (Koenigs et al., 2012; see Supplementary material for stimuli used with participants with psychopathy). Like developmental-onset ventromedial PFC injured patients, psychopathic criminals were more likely to endorse low-conflict self-serving actions, compared to non-psychopathic criminal comparison participants (OR = 3.218, P < 0.001; Supplementary Fig. 1). In conjunction with recent neuroimaging findings (Motzkin et al., 2011), the present neuropsychological data offer compelling support for the proposal that early dysfunction in the ventromedial PFC may constitute a neuropathophysiological mechanism for the development of psychopathy.

On the more ambiguous, high-conflict scenarios, comparison participants judged utilitarian actions less acceptable when they were also self-serving (e.g. pushing someone off a lifeboat to save everyone else on board including yourself versus pushing someone off a footbridge to save five strangers; Fig. 3). It seems that violating the norm against being selfish is so unpalatable that it may make an otherwise acceptable utilitarian action less acceptable. In contrast, ventromedial PFC patients (adult and developmental) endorsed the high-conflict utilitarian actions even when they might seem selfish, suggesting that ventromedial PFC damage may result in a reduced aversion to being selfish. It is possible that different pathways lead to the same atypical response pattern, e.g. disrupted integration of the aversion to selfishness into reasoning among adult-onset ventromedial PFC patients, and diminished internalization of the norms against selfishness among developmental-onset ventromedial PFC patients.

Also, as has been argued in previous studies (Koenigs et al., 2007; Thomas et al., 2011), patients with ventromedial PFC damage were more likely to endorse non-self-serving utilitarian actions, although this increase in utilitarian judgement was not statistically significant and warrants further research. Thus, ventromedial PFC dysfunction may both reduce the aversion to performing personal harms (Greene, 2007) and reduce the aversion to violating the norm against being selfish.

It will be important to continue this line of work with other types of stimuli and additional moral reasoning experiments, and to extend the findings in larger numbers of patients. We would expect the basic story line to remain unchanged—namely, that early ventromedial PFC dysfunction impairs the acquisition and maturation of moral competency that embraces the importance of considering the welfare of others, and that ventromedial PFC dysfunction (acquired at any point) disrupts the ability to integrate social-emotional information into moral judgement (Greene, 2007; Koenigs et al., 2007; Thomas et al., 2011). One interesting and open question is whether early developmental-onset ventromedial PFC damage might result in an inability to value others’ welfare at all, or, said another way, cause an insensitivity to the welfare of others no matter what is at stake—such persons might even endorse gratuitous moral violations (e.g. killing a random person for no purpose). The fact that developmental-onset ventromedial PFC patients endorsed a utilitarian action for the vast majority of the low-conflict utilitarian actions (e.g. harming one to save five), similar to comparison participants, suggests that the developmental-onset ventromedial PFC patients do appreciate others’ welfare; thus, their impairment seems to be in weighing that welfare against their own self-interest, and we would predict that they would reject gratuitous moral violations (as would adult-onset ventromedial PFC patients and healthy participants). But this is an empirical question at this point, and one that we are beginning to explore.

Our study provides novel empirical evidence that the ventromedial sector of the prefrontal cortex is critical for the acquisition
and maturation of moral judgement. In our patients, ventromedial PFC damage is macroscopic and obvious. However, early interaction of genetic and environmental factors could result in more subtle perturbations of ventromedial PFC function that could alter one’s moral developmental trajectory, creating a proclivity for antisocial and criminal behaviours. In cases of children and adolescents with elevated risk for these behaviours, interventions targeting ventromedial PFC functioning may be effective for promoting a more adaptive and prosocial moral developmental trajectory.

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Supplementary material
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References

Damasio AR, Tranel D, Damasio H. Individuals with sociopathic behavior caused by frontal damage fail to respond autonomically to social stimuli. Behav Brain Res 1990; 41: 81–94.


