NEUROSCIENCE AND THE LAW — SCIENCE AND SOCIETY

Neurocriminology: implications for the punishment, prediction and prevention of criminal behaviour

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Abstract | Criminal behaviour and violence are increasingly viewed as worldwide public health problems. A growing body of knowledge shows that criminal behaviour has a neurobiological basis, and this has intensified judicial interest in the potential application of neuroscience to criminal law. It also gives rise to important questions. What are the implications of such application for predicting future criminal behaviour and protecting society? Can it be used to prevent violence? And what are the implications for the way offenders are punished?

Advances in neuroscience are increasing our understanding of how our biology influences our behaviour — for both good and bad. The emerging field of neurocriminology seeks to apply techniques and principles from neuroscience to improve our understanding of crime, to predict crime and ultimately to prevent crime. Such an approach would have the potential economic and social benefits that are associated with violence reduction, but it also raises neuroethical concerns[1].

In this Perspective article, we discuss the current state of research in neurocriminology. We provide an overview of the neurobiological abnormalities that are associated with criminal behaviour and consider the genetic and environmental factors that may contribute to these abnormalities. We highlight studies conducted to date, many of which suggest that biological factors may aid in the prediction of future crime and violence. We then discuss implications of this research in the legal system.

The current state of neurocriminology

There are now relatively extensive literatures that document relationships between antisocial behaviour and biological functioning. With some exceptions[2], most studies are correlational and cross-sectional, and largely do not provide information on specific genetic or environmental factors that may mediate these relationships. However, an increasing number of prospective longitudinal studies are examining whether the presence of specific biological factors, such as hormone levels, neurotransmitter levels, physiological indices or brain impairments, is predictive of future offending. Because most studies define antisocial behaviour and crime broadly, without distinguishing between violent and non-violent offenders, this article largely concerns the broad propensity to criminal behaviour.

Genetics. Results from well over 100 behavioural genetics studies with different designs — including twin studies, studies of twins reared apart and adoption studies — have converged on the conclusion that antisocial and aggressive behaviour have a considerable genetic basis. Estimates of the variance that is attributable to genetics vary, but several meta-analyses place the level at between 40–60%[1]. Heritable influences, with some exceptions, are broadly consistent across gender and ethnicity[3]. Adoption studies in particular have the advantage of being able to truly separate genetic from environmental factors and provide a converging line of evidence that there are heritable influences on antisocial and aggressive behaviour (BOX 1).

Recently, research has focused on identifying which specific genes confer risk of antisocial behaviour. Several genetic variants that incrementally increase the risk of antisocial behaviour have been identified[4–7]. Although approximately one-half of 185 studies have reported positive findings, a meta-analysis revealed that no variant was associated with aggression at the 5% level of significance[8]. This finding underscores the idea that, as with other complex behaviours, the contribution of any single gene to antisocial and aggressive behaviour is likely to be quite small. It is possible that a combination of a larger number of gene variants substantially increases the risk of aggressive behaviour. Nevertheless, knowledge about individual genes may prove to be useful in improving our understanding of the mechanisms and pathways that increase the risk of antisocial behaviour. Importantly, the environment plays an equally influential part; indeed, some genetic variants confer risk of antisocial behaviour only in the presence of particular environmental risk factors, such as abuse in early childhood[9]. Research in epigenetics[10] has shown that the environment can influence how genes are functionally expressed in an individual (and even in specific brain areas); this finding undermines traditional arguments of biological determinism.

Prenatal and perinatal influences. Early health risk factors, sometimes in conjunction with social risk factors, have been found to be associated with an increased probability that a young infant will develop antisocial and aggressive behaviour. During the prenatal and perinatal period, a number of factors may be important. Birth complications, in combination with maternal rejection of the child in the first year of life, have been associated with violent criminal offending at the age of 34 years in a study carried out in Denmark[11]. This predictive finding has been replicated in the United States, Canada, Sweden and Finland with respect to violence in adulthood, and in Hawaii and Pittsburgh (USA) with respect to childhood antisocial behaviour[1]. Five other studies have shown associations between birth complications and externalizing-behaviour problems (such as aggression, delinquency and hyperactivity) in children[1]. Fetal maldevelopment during the second trimester of pregnancy, as indicated by minor physical anomalies in the child (such as low seated ears or a single palmar crease), has been associated with later violent delinquency[12] and violent offending in adulthood[13]. The association between fetal neural maldevelopment and childhood aggression and adolescent conduct disorder may be even more pronounced when combined with effects of poor parenting[14] or social adversity[15]. Criminal offending and psychopathy have been associated with another indicator of disruption in fetal development — namely, cavum septum pellucidum[16], which is the failed closure of the septum pellucidum, a process that normally takes place during gestation until approximately 6 months post-birth. Cavum septum pellucidum is thought to be an early marker for disrupted development in the limbic region of the brain[17], which in turn is associated with offending[18].

Box 1 | **Genetics and the intergenerational transmission of violence**

Jeffrey Landrigan had been adopted at birth into a loving middle-class professional family. He was nevertheless a particularly troublesome child from the beginning. This behaviour progressed from temper tantrums at 2 years of age, abusing alcohol at 10 years of age, being arrested for burglary at 11 years of age, abusing drugs as a teenager, to killing his first victim at the age of 20 years. After escaping from prison, he perpetrated his second killing and was sentenced to death. While he was on death row in Arizona for this second homicide, another death-row inmate noticed an eerie resemblance between Landrigan and Darrel Hill, an inmate he had met on death row in Arkansas. It transpired that Hill was the biological father of Landrigan — a father Landrigan had never met.

Hill, like his son Landrigan, was a career criminal who also abused drugs and also killed twice. Hill's father — Landrigan's grandfather — was also an institutionalized criminal who had been shot to death by police. Landrigan's great-grandfather was a notorious bootlegger. Hill had seen Landrigan only briefly as he hid two .38 pistols and the narcotic medicine Demerol under his baby son's mattress — an action that was unintentionally prophetic of Landrigan's future drug abuse and violence[1].

As a fourth-generation criminal, Landrigan's case documents not just the intergenerational transmission of violence but also illustrates how the adoption design separates the genetic influences of the biological parents from the environmental influences of the rearing home. Recent findings based on 43,243 adoptees and 1,258,826 non-adoptees unequivocally confirm that having a biological parent convicted of a violent crime raises the likelihood of criminal violence in the adoptee[122]. Taken together with findings from behavioural genetics studies that document heritability of aggression in children, adolescents and adults, these findings indicate that there is a genetic contribution to criminality.

Maternal nicotine consumption and alcohol consumption during pregnancy are also factors that may predispose individuals to violent offending in adulthood — findings that have been replicated across many studies in several continents[1,19]. Even small amounts of alcohol during pregnancy (one drink per week) have been associated with increased childhood aggression in the offspring[20]. There is current debate regarding whether nicotine exposure predisposes to offending by causing fetal hypoxia that results in brain impairment or whether this association is genetically mediated[21,22].

Lead levels have been associated with juvenile delinquency and aggressive behaviour in at least six studies[23]. From a prospective viewpoint, high lead levels in the mother during the first and second trimester of pregnancy are associated with an increased risk of being arrested for violent crimes in adulthood[24]. High dentine lead levels assessed at the ages of 6–9 years have been associated with increased violent offending at the ages of 14–21 years, and poorer cognitive functioning mediates this relationship[25]. Some studies that carefully controlled for potential confounds such as poverty, maternal smoking, alcohol use and drug use have shown that these findings apply to women as well as men[24,25]. Higher manganese levels in the mother during pregnancy have also been associated with increased externalizing-behaviour problems (defined as aggressive, destructive and defiant behaviour) in children aged 8–9 years[26].

Poor nutrition in either the first or second trimester of pregnancy has been associated with a 2.5-fold increase in antisocial personality disorder in the offspring[27]. Malnutrition in infancy is associated with conduct problems in adolescence, a relationship that is partly mediated by low IQ[28]. Similarly, children with signs of malnutrition at the age of 3 years have much higher rates of aggressive and antisocial behaviour at the ages of 8, 11 and 17 years[29] over and above any contribution from social risk factors. This relationship is also mediated by low IQ.

Together, these findings suggest that a number of early environmental factors may increase the risk of antisocial behaviour as late as adulthood, probably via effects on biological systems.

Hormones and neurotransmitters. The steroid hormones cortisol and testosterone have been the most intensively researched hormones in relation to antisocial behaviour. Disruptions in the hypothalamus–pituitary–adrenal (HPA) axis, the body's stress response system that regulates the release of the hormone cortisol, are frequently observed in antisocial people. Associations between antisocial behaviour and cortisol levels vary depending on the type of antisocial behaviour and other factors[30]. Psychological stress at various stages during development may produce lasting changes in HPA axis functioning and thereby predispose an individual to antisocial behaviour[31]. Low levels of cortisol in childhood are predictive of aggressive behaviour 5 years later, in adolescence[32]. Similarly, a study showed that boys who were identified as having behavioural problems and who had low cortisol levels showed more aggressive behaviour at a follow-up assessment 2 years later[33].

Increased testosterone levels have been repeatedly associated with increased aggressive behaviour in adults. Caveats include the fact that this relationship appears to be less evident in pre-pubertal individuals[31], and meta-analyses of this relationship find a small effect size of $R = 0.08$ (REF. 34). Some randomized, placebo-controlled crossover trials have shown that testosterone administration increases aggressive behaviour in adult males[35], which is suggestive of a causal connection, although other experimental studies using lower doses of testosterone did not show an increase in aggressive behaviour[36]. Increased levels of testosterone at the ages of 10–12 years are predictive of assaultive behaviour at the ages of 12–14 years, norm-violating behaviour at the age of 16 years and cannabis use at the age of 19 years[37]. Higher levels of testosterone at the age of 16 years are associated with crime in adulthood[38].

Multiple neurotransmitter systems have been implicated in aggression[39], and the best-replicated correlate of human aggressive behaviour is a low level of serotonin[40]. Low levels of serotonin in cerebrospinal fluid are a particular marker of people who show impulsive aggressive behaviour[41]. An experimental manipulation that reduces serotonin levels in the brain (that is, acute tryptophan depletion) reduced functioning of the orbitofrontal cortex during an inhibitory motor control task[42], a region commonly implicated in antisocial behaviour[43]. However, aggression has also been associated with reduced monoamine oxidase A (MAOA) levels in the brain. MAOA is an enzyme that breaks down serotonin and other neurotransmitters, and hence lower levels of MAOA would presumably result in higher serotonin levels[44]. This seemingly contradictory finding demonstrates the need for studies that simultaneously examine multiple biological markers in order to obtain information about how neurotransmitters may interact with each other to increase the risk of aggression.

Psychophysiology. Psychophysiological differences have also been observed between antisocial groups and control groups. Meta-analyses and reviews conclude that low resting heart rate is probably the best-replicated biological correlate of antisocial and aggressive behaviour in children and adolescents[45,46]. Low resting heart rate may indicate a lack of fear and a reduced likelihood of experiencing negative affect in response to a criminal act[45,46]. Low heart rate in childhood and adolescence has been associated with adult crime in all four longitudinal studies conducted to

date[45]. Across these studies, low resting heart rate was found to be as strong a predictor of future antisocial behaviour as it is of current antisocial behaviour[45]. In delinquents who were arrested for a minor offence at the age of 14 years, attenuated heart rate responses to a stressor were associated with both a shorter time to re-offend as well as with a greater number of re-offences within a 5-year period[47]. Another study showed that, after multiple confounds had been controlled for, low heart rate at the age of 18 years predicted higher conviction frequency and higher levels of violence up to the age of 50 years[48].

Psychophysiological indicators of under-arousal — such as slow-frequency electroencephalographic activity and reduced skin conductance activity — at the age of 15 years are predictive of crime at the age of 24 years[49]. A recent meta-analysis[50] has documented a reduced amplitude of the P300 event-related brain potential, which is thought to reflect inefficient recruitment of neural resources during information processing, in adult antisocial populations. Similarly, a reduced P300 amplitude at the age of 11 years has been associated with criminal offending at the age of 23 years. P300 amplitude predicted offending at the age of 23 years over and above measures of antisocial behaviour at the age of 11 years[51].

Poor autonomic fear conditioning — the ability to learn associations between neutral cues and aversive stimuli — is another well-replicated correlate of adult criminal and psychopathic adult offending[52,53], conduct disorder in children and adolescents[54,55], and juvenile offending[56]. A review of 46 human brain imaging studies suggests that deficits in fear conditioning may reflect abnormalities in a common core fear network that consists of the amygdala, insula and anterior cingulate[57]. Indeed, numerous brain imaging studies find abnormalities in these areas in antisocial people, although this has been disputed with respect to individuals with psychopathic traits[58] — a specific subgroup of criminal offenders. Poor electrodermal fear conditioning at the age of 3 years is associated with convictions for criminal offences at the age of 23 years[59]. In addition to aiding in the prediction of future offending, individual differences in fear conditioning may also provide information about which antisocial individuals may desist from future violence or be particularly amenable to treatment. For example, adolescents who were identified as being likely to commit crimes in adulthood by virtue of being antisocial at the age of 15 years but who did not go on to develop into adult criminal offenders at the age of 29 years showed superior fear conditioning compared with both antisocial adolescents who become offenders and non-criminal controls[60].

Brain imaging and neurology. Reduced functioning in the frontal lobe of the brain is to date the best-replicated brain imaging correlate of antisocial and violent behaviour. In particular, a meta-analysis of 43 structural and functional imaging studies found that the largest reductions in structure and function within the frontal lobe of antisocial individuals were observed in the orbitofrontal cortex, anterior cingulate cortex and dorsolateral prefrontal cortex[61]. The dorsolateral prefrontal cortex is associated with self-regulatory processes, including attention and cognitive flexibility, and may be linked to the antisocial features of impulsivity and poor behavioural control[61]. The anterior cingulate is involved in error processing, conflict monitoring and avoidance learning[62–64]. Individuals with damage to this region are more disinhibited and aggressive[65], and demonstrate impairments in inhibitory control and emotion processing[66,67]. The ventral prefrontal cortex, including the orbitofrontal cortex, has received particular attention given its role in emotion processing, learning from reward and punishment, and decision making[68,69].

The possibility of a causal connection between impaired orbitofrontal cortex structure and/or function on the one hand, and crime and/or violence on the other, has been raised by neurological studies showing that head injury in ostensibly normal individuals precedes the onset of disinhibited antisocial behaviour. For example, higher levels of aggression were found in war veterans who had experienced penetrating head injuries that were localized to the ventral prefrontal cortex[70]. Furthermore, neurological patients who had suffered from an accidental head injury to the ventral prefrontal cortex show poor decision making, reduced autonomic reactivity to socially meaningful stimuli and psychopathic-like behaviour[68]. In a particularly striking example, a tumour in the orbitofrontal region preceded the onset of paedophilia in an individual; after resection of the tumour, the person's behaviour returned to normal[71] (BOX 2).

The amygdala is another brain region that is consistently identified as showing altered activity in brain imaging studies of antisocial individuals. The type of deficit may vary in different subgroups of antisocial individuals. Adults and youths with psychopathic traits, who have blunted emotional responding and may engage in more cold, calculated aggression, have reduced amygdala volume[72] and functioning[73–75], whereas individuals with a more impulsive, reactive form of aggression demonstrate exaggerated amygdala reactivity[76]. Reduced amygdala volume in psychopathic individuals has been localized to the basolateral, lateral, cortical and central nuclei — regions that are involved in emotion processing, fear conditioning and autonomic reactivity to affective stimuli[72]. Of note, patients with damage to the amygdala have a reduced sense of danger, are less fearful[77] and have deficits in the recognition of fearful facial expressions[78] (a process involved in experiencing empathy). The association noted earlier[59] between poor classical conditioning in childhood and crime in adulthood suggests, but does not prove, a causal relationship between amygdala functioning and antisocial behaviour.

Most brain imaging studies are essentially correlational and cross-sectional, and until recently no longitudinal brain imaging research on antisocial populations has been conducted. Two recent studies have indicated the potential for neuroimaging to provide incremental predictive power in predicting re-offending. One study showed that reduced functioning in the anterior cingulate during a go–no-go task in prisoners doubled the likelihood of re-arrest 3 years later[79]. A second study of high-risk community males showed that reduced amygdala volume at the age of 26 years was associated with violent offending 3 years later[18]. As has been observed in other biological longitudinal research, both studies showed predictive utility of brain measures over and above past history of antisocial behaviour and other confounds.

Other longitudinal studies have shown that incurring brain damage increases the risk of criminal behaviour. A longitudinal study of 231,129 individuals from Sweden documented a threefold increase in violent crime after traumatic brain injury (TBI) after adjusting for demographic confounds[80]. A prospective longitudinal study of 12,058 individuals from Finland showed that TBI during childhood and adolescence was associated with a 1.6-fold increase in crime in adulthood after controlling for confounds; children suffering from TBI before the age of 12 years started their criminal careers significantly earlier than those who suffered from TBI after the age of 12 years[81]. These studies demonstrate that information about brain structure and function, regardless of whether the origins are neurodevelopmental or a result of a direct physical insult later in life, may be of some use in identifying which individuals are at an increased risk of criminal behaviour.

Box 2 | **Ventral prefrontal dysfunction, paedophilia and legal responsibility**

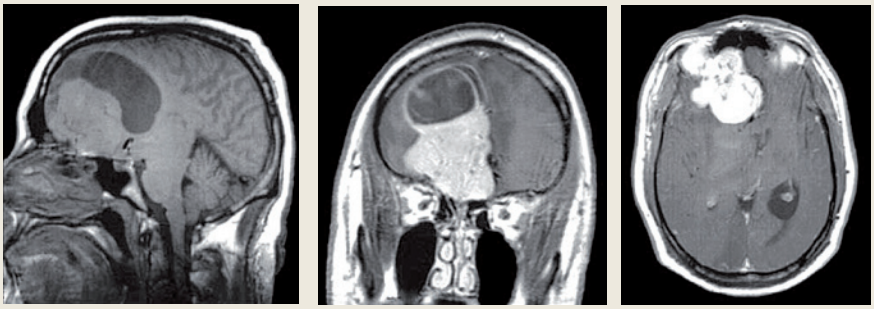
Cross-sectional brain imaging studies are correlational and cannot prove a causal association. Individual case studies can, however, be suggestive of causality.

Michael was a 40-year-old schoolteacher and past correctional officer. He was happily married to his wife and loved both her and Christine, his stepdaughter. He had no prior history of criminal or deviant behaviour. However, Michael began to change. He became uncharacteristically aggressive with his wife and began taking pornography to school. His bedtime rituals with his pre-pubescent stepdaughter, which had previously consisted of singing lullabies, became more sordid, and he eventually got into bed with her. He was found out and convicted of child molestation.

Michael had to decide between a prison sentence and a treatment programme. He chose the treatment programme but was expelled after propositioning female staff. The night before he was due to be transported to prison, he went to the emergency room complaining of a severe headache. There he continued to solicit sexual favours from staff.

An astute neurologist ordered an MRI scan after Michael wet his trousers without showing any apparent concern. The MRI revealed a tumour growing from the base of the orbitofrontal cortex (see the figure, which shows MRI scans of Michael's brain at the time of the initial neurological evaluation, revealing a tumour mass displacing the right orbitofrontal cortex). After the tumour was resected, Michael's behaviour returned to normal, and he was reunited with his wife and stepdaughter. After several months of normal behaviour, his wife discovered child pornography on his computer. Michael was re-examined, and it was discovered that the tumour had regrown. It was resected for a second time, and for at least 6 years after the resection Michael's behaviour has returned to normal[1,71].

The case comes almost as close as one can get to a causal connection between ventral prefrontal brain pathology and deviant behaviour — a pendulum moving from normality to brain dysfunction to paedophilia to neurosurgery to normality, and back again. In the face of the order in which events occurred, was Michael responsible for his inappropriate sexual behaviour with his stepdaughter?



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Remaining challenges for research on biological risk factors for violence and crime. In sum, in recent years, evidence of the importance of biological factors in antisocial behaviour has accumulated and is being recognized as valuable in our understanding of crime and violence. With advances in neuroscience and the design of longitudinal investigations, studies are becoming methodologically stronger. Taken together, it is becoming increasingly harder to argue that biological factors do not predispose some individuals to adult crime. This conclusion neither diminishes nor replaces social and environmental perspectives on crime causation[24,29,80]. Together, genetic and environmental factors shape the way that biological systems develop and function, and thus affect multiple complex psychological processes that are important in controlling and regulating behaviour and in behaving morally.

Important gaps in our knowledge remain. Very little is known about the neurobiology of regulatory crimes, and one study showed increased cortical thickness and better prefrontal functioning, as opposed to impairments, in white-collar criminals[82]. A future challenge in neurocriminology lies in parsing out the specific genetic and environmental influences that induce neurophysiological changes that result in the more proximal cognitive, affective and behavioural risk factors for violence. In other words, what neurobiological processes mediate the relationship between the well-documented early social risk factors and violence in adulthood?

A few studies have begun to explore how genetic and environmental factors affect the brain. For example, researchers have found that the adolescent offspring of mothers who smoke during pregnancy have reduced thickness in two regions of the brain that have been implicated in antisocial behaviour — the orbitofrontal cortex and middle frontal cortex[83]. Children exposed to high levels of lead early in life have been shown in adulthood to have reduced grey matter volume in the brain, particularly in the prefrontal cortex[84]. Males with a common polymorphism in the *MAOA* gene (which is present in about 30% of the population) have an 8% reduction in the volumes of the amygdala, anterior cingulate and orbitofrontal cortex[85], which suggests that there is a causal pathway from genes to brain to antisocial behaviour. To delineate these types of causal connections, future studies need to examine the pathways by which genes and the environment affect biological systems, and how these altered systems in turn predispose individuals to antisocial behaviour.

A predisposition to criminal behaviour is unlikely to be reduced to one or even two simple brain circuits but probably involves multiple brain dysfunctions and multiple circuits that each give rise to different risk factors for violence. Thus, the future use of brain imaging in the assessment of risk of criminal behaviour will require a much more sophisticated understanding of these circuits. Although brain imaging techniques have advanced rapidly in the past few decades, there are still many limitations to these methods[86]. However, with continued methodological improvements in neuroscience research, we will gain more information about how brain regions function together to predispose individuals to criminal behaviour.

Although only a few prospective studies have been conducted, findings from research on early risk factors suggest that information about biological factors in youths may aid in the prediction of which individuals are more likely to engage in crime and violence later in life. Such information may also help to identify individuals who are particularly amenable to rehabilitation. In a review of ten studies implementing variants of cognitive–behavioural therapy in individuals with antisocial behaviour[87], multiple neurobiological factors were predictive of treatment response and progress, including heart rate, hormone levels and neuropsychological measures of risk taking, sensitivity to negative consequences, impulsivity, cognitive flexibility and emotion processing. Although such initial findings are provisional, these neurobiological characteristics could ultimately help to determine which offenders are best suited to specific rehabilitation programmes and are more likely to re-integrate into society

safely. A major challenge that remains to be addressed is the identification of socially acceptable psychosocial or biological intervention programmes that target biological risk factors for criminal behaviour.

The legal context

Neurocriminology interfaces with the judicial system at three main levels: punishment, prediction and prevention. To what extent does the growing body of knowledge on the neuroscience of crime and violence suggest that we should rethink our approach in these three domains? Although it is unlikely that neurocriminology will result in any radical or swift shift in the operation of the criminal justice system in the very near future, it is not inconceivable that some modest change may occur in these areas at some point, assuming that the field continues to develop and evolve, as the past two decades have suggested.

Punishment. Punishment is predicated on blameworthiness, and the extent to which we blame individuals is a function of the extent to which they can be held accountable for their actions. Such accountability in a legal context is based on the concept of responsibility.

In this context, let us assume that, to some extent, neurobiological abnormalities or insults relatively early in life predispose some individuals to a life of crime and violence. We also assume that offenders are not responsible for being exposed to these early risk factors for violence. So are these offenders responsible for their behaviour, and if so, to what degree? In the case of Michael, in whom a tumour in the orbitofrontal region preceded the onset of paedophilia, which disappeared after the tumour had been removed[71] (BOX 2), the question was: was he responsible for his paedophilia? Currently, in the United States, an individual is deemed 'responsible' for their actions if two conditions are met: first, they have sufficient rational capacity; and second, they are not acting under coercion. Rational capacity is typically interpreted as whether the individual knew what he or she was doing and understood that his or her actions would have consequences. Michael's (BOX 2) is a telling case because the temporal ordering of events — from normality to brain tumour to paedophilic interest to tumour resection to normality, and back again — is suggestive of causality in this particular case. However, in his own words, Michael admitted, "…somewhere deep, deep, deep in the back of my head, there was a little voice saying 'You shouldn't do this'" (REF. 88). He knew at the time of the act what he was doing, and he also knew that what he was doing was wrong. In the eyes of the law, Michael was legally responsible for his actions.

Given that Michael would be considered legally responsible, it is difficult to argue that someone with a less obvious neurobiological 'predisposition' to offending than that of Michael — such as reduced functioning of the amygdala during a moral decision-making task, carrying a specific variant of the *MAOA* gene or a significant but non-obvious volume reduction in prefrontal grey matter — is not responsible for his or her actions. In most criminal cases, the causal flow from biological risk to offending will never be known. All behaviour has a cause, and identifying the neural basis of a behaviour in an individual does not in itself establish that the individual had diminished rational capacity[89]. Therefore, as the law currently stands in the United States and other countries, the documentation of neurobiological risk factors, no matter how early they originated, does not render that individual lacking responsibility.

Despite this current legal stance, a challenging question concerns whether the current law pertaining to responsibility is in need of modest revision. This is ultimately a normative question over which there can be reasonable disagreement. Even without invoking the presence of biological risk factors to suggest impaired rational capacity, it has been argued that severe psychopaths should not be held responsible on the grounds that they have no sense of moral rationality — they are not sensitive to moral concerns and thus do not have the same moral sense as most people in society[90]. When one considers in addition an increasing body of evidence showing that neurobiological factors contribute to criminal psychopathy in adults as well as to behaviour in children with psychopathic-like traits[91], such a revision perhaps becomes more compelling, particularly in a case in which an individual has several documented neurobiological and psychosocial risk factors for violence potential, as in the case of Donta Page (BOX 3).

The judicial system acting in a practical world essentially conducts binary decision making: for example, in establishing innocence versus guilt. Determination of diminished capacity in the United States similarly involves a categorical judgement on the presence or absence of a mental disability. The fairness of this binary judgement can be reasonably questioned. The widespread consensus of experts is that crime and antisocial behaviour are dimensional, and not categorical, constructs[92]. Risk factors associated with antisocial and criminal violence are also usually dimensional in nature (for example, the degree of prefrontal dysfunction and the resting heart rate), although some may be categorical (for example, the presence of TBI or genetic polymorphisms). Unlike in the United States, the judicial practice in the Netherlands is guided by a five-point scale for assessing the degree of criminal responsibility, with evaluations including personality and neuropsychological testing[93]. Thus, although neuroscience has no current definitional bearing on concepts of responsibility, it is not without international precedent to consider a revision to legal practice in the United States, United Kingdom and other countries so that responsibility may, in the future, be assessed on a continuum using measures that include neurobiological variables.

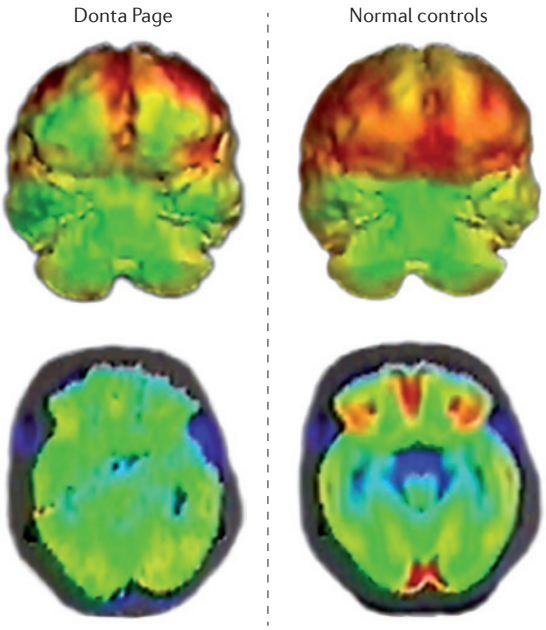
Although a sensible dividing line needs to be drawn for practical reasons, in theory one can conceive of a set of multiple neurobiological and genetic influences that, combined with social influences, diminish responsibility to varying degrees. To the extent that neuroscience provides reliable methods to document these influences objectively, and assuming that methodologies become less expensive and quicker and easier to implement than hitherto, we anticipate that responsibility will eventually be conceptualized more broadly than it is today. For example, although cognitive intelligence is the benchmark used by the law to document the capacity for rationality, the relatively new fields of affective psychology and affective neuroscience are providing us with evidence that emotion informs decision making[68,94] — a finding that is not yet instantiated in the law. Can individuals therefore be fully responsible when the feeling for what is moral is diminished? What may be just as important as knowing the difference between right and wrong when making moral decisions is having the feeling of what is right and wrong. As recent studies have documented in psychopaths, some individuals may have deficits in brain regions that are important for generating these emotional responses (BOX 4).

The facts that research in the field uniformly recognizes substantial affective impairments as a core feature of psychopathy and that there is no longer any reasonable doubt that such affective impairment influences behaviour[95,96] raise the question of whether the legal system will eventually reformulate its current, long-standing concept of responsibility. For example, environmental head injuries can change an otherwise responsible individual into a person

Box 3 | **Neuroscience in the courtroom**

Donta Page, a young African-American male, brutally raped and murdered Peyton Tuthill, a young white woman living in Denver (Colorado, USA) in 1999. The defendant was brought across state lines to be scanned in the same positron emission tomography scanner with the same challenge task used in one prior study that had shown prefrontal dysfunction in murderers[11]. A comparison of the defendant's brain scan with the average of 56 normal control individuals showed reduced activation in the ventrolateral, ventromedial and polar prefrontal cortex (see the figure, which shows reduced functioning of the ventral prefrontal cortex in Page's scan (left) compared with normal brains (right)). The author (A.R.) testified in the ensuing court case that such brain dysfunction, which potentially arose from documented severe physical abuse and head injuries in childhood, could predispose to poor decision making, lack of self-insight, lack of affect and poor behavioural controls, which in turn predisposes to callous, disinhibited behaviour. Inter-racial homicide is relatively rare and may have polarized the jury, who found the defendant guilty of first-degree murder with deliberation, punishable by death. In the death penalty hearing, a three-judge panel accepted the reasoning that impaired capacity due to brain dysfunction — in conjunction with multiple additional biosocial predispositions to violence that included parental neglect, extreme poverty, sexual abuse, poor nutrition, low heart rate and lead exposure — had probably limited the defendant's ability to appreciate the wrongfulness of his acts. He was spared the death penalty and given life imprisonment.

This case highlights two competing perspectives on the application of reductionist neuroscience knowledge to the practical, life-or-death issue of criminal responsibility. If an individual is burdened early in life with biological and social risk factors beyond their control, which, in a probabilistic fashion, increase the likelihood of a criminal lifestyle, are they fully responsible for their homicidal actions? Conversely, all behaviour has a cause that is founded in the brain. Just because a putative causal path has been documented, should it be exculpatory? Would such exculpation erode our concept of moral responsibility?



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who, although cognitively capable of differentiating right from wrong, lacks the neural regulatory affective and behavioural control over their behaviour[97]. It has been suggested that as neuroscience begins to offer a more detailed and specific account of the physical processes that can lead to irresponsible or criminal behaviour, the public perception of responsibility may begin to change in the same way that public viewpoints on addiction have shifted from addiction as a failure of personal responsibility towards addiction as a disease[98].

Prediction. If biological factors could predict future violence over and above predictions based on social variables, even opponents of a neuroscientific perspective on crime would have to agree that neurobiology has added value in this area. Whether or not such biological factors are causes or merely correlates of violence is irrelevant to the issue of prediction — the fact that they add predictive value is the currency of risk assessment in prisoners who are about to be released.

Given that approximately 50% of the variance in aggressive and antisocial behaviour can be explained by genetic influences, a compelling case could in theory be made for using biological information to improve violence prediction. However, the fact that molecular genetic studies have so far largely failed to identify specific genes that can account for more than 1% of the variance in any complex behavioural trait gives considerable pause for thought[99,100]. Molecular genetic advances have, in theory, the potential to elucidate and identify specific genetic factors that predispose individuals to crime in the future, but currently the value of genotyping individuals to predict future violence is limited.

Perhaps surprisingly, endophenotypes such as prefrontal dysfunction and low heart rate, which reflect compound genetic and environmental influences, may currently explain more of the variance in adult violence than any individual genotype and may have more traction in predicting future violence. The literature reviewed above has revealed several replicable early biological correlates of later violence. Some studies have shown that neurobiological markers can predict, over and above well-replicated psychosocial risk factors, which individuals will demonstrate antisocial or psychopathic traits[101,102]. The two recent imaging studies described above[18,79], together with multiple studies that have identified psychophysiological and hormone predictors of future offending, provide some support for the conclusions made in a Royal Society report that neuroscience may have future value in predicting re-offending[103].

Despite the potential promise, and indeed likelihood, that neurobiology could provide at least modest increases in predictive power, methods used to predict the potential of future re-offending in about-to-be-released prisoners have so far never incorporated neurobiological markers into the risk assessment equation. There are three main reasons for this. First, the evolving body of knowledge on neurocriminology has not yet been accepted in the social sciences and among practitioners. Second, neurobiological measures are less easy to collect than behavioural, social and psychological data. Third, there have been longstanding ethical concerns about collecting biological data on offenders. This may change given that DNA is now collected on all arrestees in the United States. Technical developments are also increasingly making neurobiological risk assessments more feasible and practical, and some, such as the measurement of resting heart rate, are already incorporated into standard medical practice at the community level.

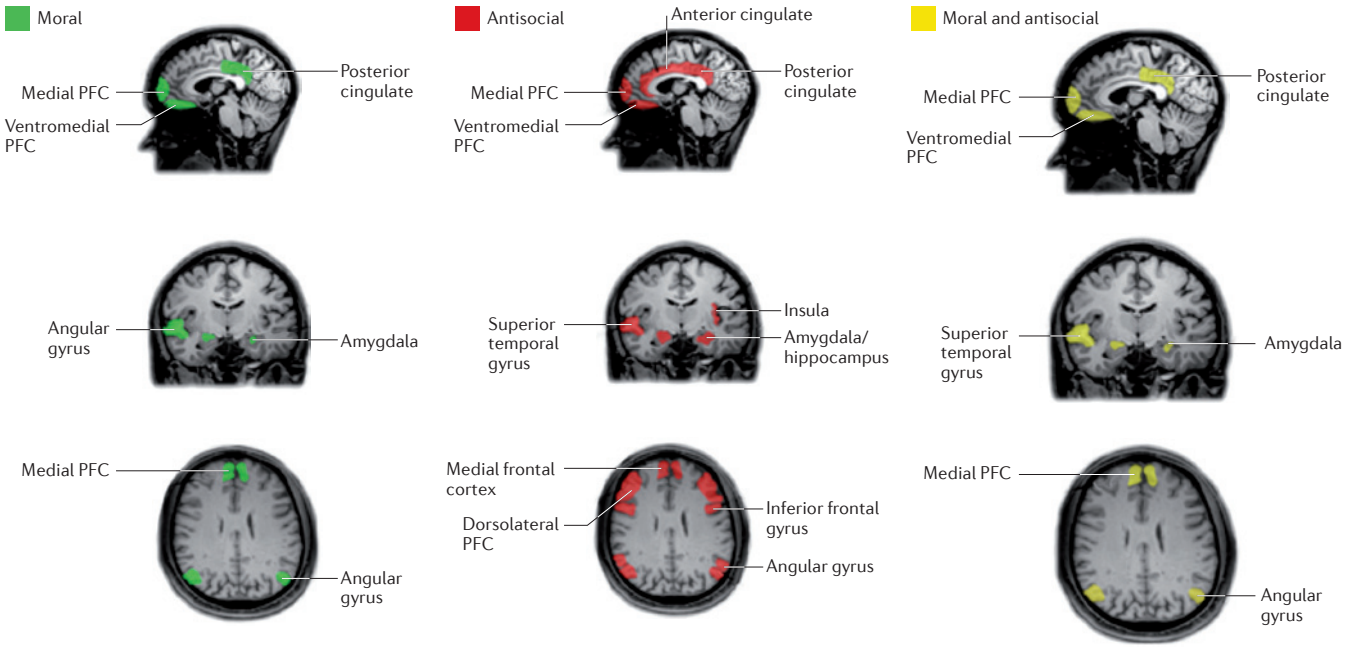
Any major advances in predicting future violence will be based not just on progress in neurocriminology but also on statistical advances. Machine-learning techniques such as random forest have already been documented to improve the prediction of future charges of homicide or attempted homicide using traditionally available demographic and social variables[104]. If neurocriminology can identify replicable biological risk factors that provide incremental knowledge

Box 4 | **Common neural circuits in moral decision making and antisocial behaviour**

Although criminal offending is heterogeneous in nature, a common denominator is that it is immoral. It is conceivable that the neural circuitry underlying moral decision making is impaired in offenders. This moral neural circuit is broadly comprised of the polar and medial prefrontal cortex (PFC), ventral PFC, angular gyrus, posterior cingulate and amygdala. These brain regions have substantial overlap with those regions that are found to be structurally or functionally impaired in offenders[123] (see the figure, which shows a schematic diagram of brain regions that are activated only in moral decision making (green), regions that are impaired only in antisocial groups (red), and regions common to both antisocial behaviour and moral decision making (yellow)). This overlap gives rise to the 'neuromoral' hypothesis of antisocial behaviour, which states that some of the brain impairments that are observed in antisocial individuals disrupt moral emotion and/or decision making, thereby predisposing individuals to rule-breaking, antisocial behaviour[1].

This raises an intriguing forensic question. There is little doubt that most violent psychopaths 'know' the difference between right and wrong — but do they have the 'feeling' of what is right and wrong? Moral decision making is viewed as being influenced by affect[68,94]. This 'moral feeling', which is centred partly on the amygdala, is argued to be the engine that translates the cognitive recognition that an act is immoral into behavioural inhibition — a mechanism that functions less well in affectively blunted antisocial individuals. Impairments to the emotional component that comprises the feeling of what is moral are viewed as a core feature of psychopaths and are also present in other offenders.

Thus, if a criminal offender has documented disruption to this moral neural circuitry and lacks the feeling for what is right and wrong, are they fully accountable for their immoral behaviour? If this moral circuitry can be better delineated and quantified at the individual level in the future, this affective metric could be entered as a mitigating factor in the punishment phase of a trial, just as low IQ — a cognitive metric — is currently used to establish lack of rational capacity and to excuse the defendant in the guilt phase of a trial.



over and above the traditional variables that are currently used in dangerousness assessments, this would further aid violence prediction. Indeed, given that probation and parole decisions must be made every day in offender populations, and assuming that neurobiological data can reliably enhance the accuracy of such predictions, it could be viewed as ethically questionable not to use such knowledge. However, such a development would raise several powerful ethical concerns. The potential for future extension of such predictions from offender populations to non-offender community populations is one such concern given the egregious civil liberty violations that could arise from false positives — that is, non-dangerous individuals being predicted to be at risk of committing crimes.

Intervention and prevention. If neurocriminology could provide even very modest insights into how future offending can be reduced, it would gain considerable traction in the contexts of law and society in general, given that rehabilitation is a consideration in sentencing criminal offenders. Research in this area is currently sparse, but some studies suggest that neurobiological research can inform practice and provide guidelines for future research.

At the psychopharmacological level, it is known from over 45 randomized controlled trials that that a wide range of medications — including atypical antipsychotics, mood stabilizers, stimulants and antidepressants — are effective in reducing aggressive behaviour in children and adolescents[105]. Although such effects may in part be due to the treatment of clinical conditions that are co-morbid with aggressive behaviour, such as attention-deficit hyperactivity disorder and depression, pharmacological intervention is also effective in children presenting solely with aggressive symptoms. In adults with impulsive aggression, treatment with selective serotonin reuptake inhibitors has been found to increase glucose metabolism in the orbitofrontal cortex[106], suggesting a potential method for improving functioning in regions that have been identified as deficient in antisocial populations.

Despite these findings, there appear to be few, if any, systematic studies on the long-term efficacy of medications or their application to offender populations. Controversially, anti-androgen medications

such as medroxyprogesterone or Depo-Provera are thought to reduce recidivism in sex offenders[107], but well-controlled randomized controlled trials are lacking. There is agreement that anti-androgens do reduce sexual drive, and in practice at least eight states in the United States have laws on chemical castration. Although some have argued that chemical castration violates the constitutional rights of the offender, others have countered that these medications are effective, that offenders are capable of making an informed decision and that preventing such informed choices that have appropriate safeguards in place is ethically questionable[108].

A more socially acceptable avenue of biological intervention may lie in nutritional supplementations such as omega-3 fatty acids. Several studies have documented initial effectiveness in reducing antisocial and aggressive behaviour in child and adult populations[109–111], although null findings exist[112]. The only two randomized controlled trials conducted in prison populations have documented a 34–36% reduction in serious offending in young offenders[109,110]. Long-chain fatty acids are critical for brain structure and function; they constitute 30% of the cell membrane and are known to enhance neurite outgrowth and prolong cell life[113]. Given the existence of structural and functional neural correlates of antisocial and violent behaviour and the finding that poor nutrition is an early risk factor for antisocial and aggressive behaviour, omega-3 supplementation may prove to be modestly beneficial for at least some subgroups of offenders.

From a public-health perspective, applications of neurobiological research on violence at the population level relatively early in life may help to prevent adult violence. In one randomized controlled trial, low-income pregnant mothers were provided with prenatal and early postnatal home visitations from nurses who gave advice on reducing smoking and alcohol use and improving nutrition. The study documented a 63% reduction in the number of convictions among the 15-year-old children of these mothers[114]. One experimental environmental enrichment programme that provided better nutrition, more physical exercise and cognitive stimulation to community children aged 3–5 years documented increased electrocortical arousal and autonomic orienting at the age of 11 years[115] and a 34.6% reduction in offending rates at the age of 23 years[116]. In principle, targeted investment of resources to underserved populations at risk of future violence has the potential to enhance neurocognitive functioning and prevent offending, although these initial public health prevention programmes require replication and extension.

Novel, innovative approaches to crime prevention through benign brain manipulation also have the potential to develop from basic neuroscience research. One recent experimental transcranial direct-current stimulation study showed that enhancing neural excitability of the right lateral prefrontal cortex increases compliance to social norms enforced by punishment[117]. Because crime is a failure to comply with punishment-enforced social norms, and as brain imaging research has documented reduced lateral prefrontal functioning in antisocial groups[61], enhancing prefrontal function could, as argued by others, have implications for crime prevention, albeit at a potential cost of reduced compliance to norms that are not sanctioned by punishment[117]. Mindfulness training has also been experimentally shown to enhance both prefrontal and amygdala functioning[118,119], and has been claimed to reduce aggression in offenders[120,121]. We caution that this potential for crime prevention is extremely preliminary but logically follows from our review of biological risk factors, legal implications and prevention measures. Many would agree that once we can successfully treat offenders, important changes in the law and our social perspective on crime will inevitably ensue.

Conclusions and future directions

Neurocriminological research in particular, and neuroscience in general, are not yet poised to make immediate changes in the prediction, prevention and punishment of criminal offenders. It is also unclear how strong and how well replicated scientific findings should be for their proper use in legal cases, although most evidence can be entered as mitigating factors in the penalty phase of a capital punishment case. At the same time, notwithstanding difficulties in determining causality, there is increasing convergence from different disciplinary perspectives that neurobiological influences partly predispose an individual to offending. It is our considered opinion that it would be valuable for researchers and practitioners to focus efforts on: first, the development of innovative and benign biological programmes for crime prevention; second, attempting to enhance the prediction of recidivism, with socially acceptable accuracy, by including neurobiological predictors; third, including emotion alongside cognition in how we legally conceptualize responsibility; fourth, considering the adoption of a dimensional concept of partial responsibility; and fifth, discussing the thorny neuroethical implications of this growing body of neurocriminology research that include the potential for conceptualizing crime as having a physical cause (for example, viewing crime as the result of psychological deficits), stigma and labelling (that is, the potentially harmful effects of identifying individuals based on early biological predispositions)[98]. In conclusion, there is initial proof of concept that neuroscience can become an important future influence in society's approach to the punishment, prediction and prevention of criminal behaviour.

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Competing interests statement
The authors declare no competing interests.

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