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The frontal cortex and the criminal justice system

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In recent decades, the general trend in the criminal justice system in the USA has been to narrow the range of insanity defences available, with an increasing dependence solely on the *M'Naghten* rule. This states that innocence by reason of insanity requires that the perpetrator could not understand the nature of their criminal act, or did not know that the act was wrong, by reason of a mental illness. In this essay, I question the appropriateness of this, in light of contemporary neuroscience. Specifically, I focus on the role of the prefrontal cortex (PFC) in cognition, emotional regulation, control of impulsive behaviour and moral reasoning. I review the consequences of PFC damage on these endpoints, the capacity for factors such as alcohol and stress to transiently impair PFC function, and the remarkably late development of the PFC (in which full myelination may not occur until early adulthood). I also consider how individual variation in PFC function and anatomy, within the normative range, covaries with some of these endpoints. This literature is reviewed because of its relevance to issues of criminal insanity; specifically, damage can produce an individual capable of differentiating right from wrong but who, nonetheless, is organically incapable of appropriately regulating their behaviour.

Keywords: prefrontal cortex; volition; limbic system; frontal disinhibition

1. INTRODUCTION

It is the duty of every academic to argue for the importance of their field, and to tout the recent advances and expansion that it has undergone. Despite the clichéd ubiquity of this pattern, I believe that neuroscience and our understanding of the functioning of the brain has undergone a particularly dramatic example of this expansion. As one measure of it, the annual meeting of the Society for Neuroscience, arguably the premier general neuroscience conference, attracts some 25 000 attendees and features some 14 000 poster or lecture presentations. Many of these subjects concern deadening minutia (except, of course, to the three people on Earth feverishly taken with that topic), but some findings in neuroscience should seem nothing short of flabbergasting to any intelligent person.

In some instances, these findings must challenge our sense of self. Some examples are listed below.

(i) Huntington's disease is a neurological disorder in which there is extensive damage to the extrapyramidal motor system in the brain, producing choreic writhing throughout the body, typically starting around the age of 40 years. In a sizeable percentage of patients, these motoric symptoms are preceded a few years earlier by damage to the frontal cortex and associated changes in personality. Such changes typically involve marked social disinhibition, increases in aggressiveness and hypersexuality, patterns of impulsivity and poor social judgement. Because of these features, those with Huntington's disease are often initially diagnosed with a psychiatric disorder (Cummings 1995). Remarkably, Huntington's disease is a result of a single gene mutation. In other words, alter one gene among tens of thousands and, approximately halfway through one's life, there occurs a dramatic transformation of personality.

(ii) Transgendered individuals feel themselves to have been born into a body of the wrong gender, and explanations for this phenomenon have been put forth by various professionals, including endocrinologists, psychoanalysts and developmental biologists. A recent study forces a rethinking of transgenders. There exists a particular nucleus within the hypothalamus of the brain that is sexually dimorphic; there is a pronounced and consistent difference in the size of the nucleus, depending on the gender of the person. Among transgendered individuals, this nucleus has been reported to be the size typical not of the gender of that person, but of the gender they have always felt themselves to be. This is observed whether or not the person actually has undergone a sex change operation and the accompanying hormone treatments. Thus, despite being a particular gender at the level of one's chromosomes, gonads, hormones, phenotype and by one's treatment by society, some individuals, nonetheless, feel themselves to be of the other gender... and this area of the brain agrees. Thus, the issue with transgenderism may not be that someone feels that they are of the wrong gender: instead, it may be that someone has the body of the wrong gender (Kruijver *et al.* 2000).

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(iii) Mammalian species differ as to whether they are monogamous or polygamous (and where genetic, anatomical and ethnographic data in humans suggest that we hover somewhere in between, being neither fish nor fowl). Some recent work has uncovered the neurobiological basis of monogamy in some rodent species. In the males of these species, repeated mating with a female triggers release of the hormone vasopressin. Ample quantities of vasopressin receptors occur in a brain region called the nucleus accumbens of such males (but not in the nucleus accumbens in closely related rodent species that are polygamous). This nucleus plays a central role in mediating pleasure, and the vasopressin activates this pathway, causing the male to associate those pleasurable feelings with that particular female, thereby cementing them into a pair-bond. Remarkably, 'gene therapy' techniques can be used to overexpress vasopressin receptors in that part of the brain in a male rodent of a polygamous species, thereby shifting them to monogamous behaviour (Lim *et al.* 2004).

(iv) Finally, one subtype of epilepsy, centred in the temporal lobe, causes an array of subtle personality changes that are a function of the type of epilepsy itself (rather than of merely suffering from a serious disease). Among these changes is, typically, a preoccupation with religious and philosophical subjects (Waxman & Geschwind 1974).

In other words, neurobiology is beginning to provide the first hints of mechanistic explanations for our personalities, propensities and passions.

These insights can be of extraordinary relevance, in that neurobiology often must inform some of our decision making. Is a loved one, sunk in a depression so severe that she cannot function, a case of a disease whose biochemical basis is as 'real' as is the biochemistry of, say, diabetes, or is she merely indulging herself? Is a child doing poorly at school because he is unmotivated and slow, or because there is a neurobiologically based learning disability? Is a friend, edging towards a serious problem with substance abuse, displaying a simple lack of discipline, or suffering from problems with the neurochemistry of reward?

Issues such as these prompt that chauvinistic sense on my part that a knowledge of neurobiology would make all of us better informed voters, family members and teachers.

Arguably, the most important arena in which a greater knowledge of neuroscience is needed is the criminal justice system. In some cases, the criminal justice system has accommodated well the lessons of neurobiology. If someone with epilepsy, in the course of a seizure, flails and strikes another person, that epileptic would never be considered to have criminally assaulted the person who they struck. But in earlier times, that is exactly what would have been concluded, and epilepsy was often assumed to be a case of retributive demonic possession (Eadie & Bladin 2001). Instead, we are now a century or two into readily dealing with the alternative view of, 'it is not him, it is his disease'.

However, there are an ever-increasing number of realms in which the legal system has made little headway in incorporating neurobiology. In this paper, I consider some of the greatest incompatibilities between these two realms and some of the most important ways in which modern neurobiology can inform criminology, with an emphasis on the role of impaired volition in the insanity defence. First, two caveats: I write this as a scientist, and thus readily anticipate that some of the representations of the legal realm will be grossly simplified. Second, I write as an American, which means that the criminal justice system that I am most familiar with has some rather unique features to it. This includes a society with extremely high rates of violence, of incarceration and of recidivism, a propensity virtually unmatched in the Judeo–Christian world for executing criminals (coupled with frequent cases of conviction of the wrong person in capital cases (Acker *et al.* 2001)), and well-documented patterns in which the likelihood of conviction and the severity of punishment differ systematically as a function of the ethnicity and socioeconomic status of perpetrators and/or victims.

2. THE WORLD OF SCIENCE VERSUS THE WORLD OF LAW: CATEGORIES, CAUSALITY AND CONTINUA

Before considering the heart of this paper, namely the neurobiology of impulse control and its relevance to issues of criminality, it is important to first consider some cultural differences between the legal world and that of science. The most fundamental one reflects a luxury available to the basic scientist that is not available to a juror. For the scientist, a world of uncertainty and imperfect evidence is the fuel that drives the next study and the next hypothesis, leading to an ever more nuanced and complex sense of how something works. This is the basis of the quip that science consists of people learning more and more about less and less. By contrast to this luxury of time, for a juror, a world of uncertainty and imperfect evidence must nonetheless still be navigated to produce a decision. Two other contrasts, now discussed, may be less obvious.

(a) *Thinking (and judging) in categories versus in continua*

A second tension between the legal and scientific worlds concerns the topic of categorical thinking. As the joke goes, the world can be divided into two types of people, namely those who divide the world into two types of people and those who do not. There can be an immensely strong cognitive pull to operate in the former way, in terms of labelling, categorizing and dichotomizing, despite the fact that so many phenomena that we are exposed to occur as continua. Labels and boundaries that break continua into cognitively digestible units aid our memory, and many neurons in associational cortical regions respond to stimuli in a categorical manner.

Despite this pull, categorical thinking distorts our ability to view accurately the relationships among facts, in that we tend to underestimate the difference between two facts that happen to be given the same categorical label, while we overestimate the difference between the same two facts if they are given different categorical labels. This was shown in one remarkable study in which 'categorical' neurons were identified in the cortex of monkeys which would respond to the image of a dog or a cat (but not both). The experimenters then presented the test subjects with a computer-generated image of a cat or dog, and then would slowly morph the image so that it was a hybrid of the two (where the image could be, for example, 90% dog and 10% cat,

and so on). They found that species-responsive neurons maintained a fairly consistent level of responding as the percentage of the image derived from that animal dropped from 100%, until there was an abrupt transition of responsiveness around the 50% mark. In other words, a neuron 'considered' a 60% dog to have more in common with a 100% dog than with a 40% dog (i.e. neurons themselves underestimate differences within category, and overestimate differences between categories (Freedman *et al.* 2001)).

Good scientists typically struggle to think in continua, a style that is a logical extension of thinking probabilistically. And this awareness of continua permeates all of the life sciences, stretching from determining when life or foetal viability begins to when life ends.

Of necessity, this cognitive style must butt heads with categorical demands in many settings. For example, total cholesterol concentrations of 199 and 200 do not differ in a biologically meaningful way; however, only the latter commands the label of 'elevated'. Scientifically informed clinicians incorporate the irrelevance of such categorical boundaries into their thinking, but insurance companies often do not. This is particularly problematic in the realm of medicine that is most intrinsically built on continua, namely psychiatry. This is seen with genetic aspects of psychiatry where, for example, there is a smooth genetic continuum between schizophrenia, a disorder of wildly disruptive delusional thinking, and schizotypalism, in which there are far milder 'metamagical' delusions. Or consider the obvious continuum between the severity and duration of bereavement grief that counts as 'normal' and that which is categorized as segueing into a major depression. The Diagnostic and Statistical Manual of the American Psychiatric Association is the bible of the field and is structured categorically, partly reflecting the cognitive pull of categorization as well as the exigencies of insurance reimbursement. Currently, its editors are struggling, in preparing the next edition, with converting diagnosis from a categorical structure to one of continua (Helmuth 2003).

Thus, this cultural feature of many types of science must be utterly at odds with the legal world in which continua must be broken into the sharpest and most consequential of dichotomies: guilty versus not guilty.

(b) *A cause versus multiple and interactive causes*

A belief that it is possible to make categorical judgements can readily lead to having problems with some aspects of causality. One version concerns the difficulty in dealing with the situation in which one agent causes diffuse, statistical harm. This might be the case in a scenario in which some industrial polluter is found to have been illegally dumping a toxin into the water supply. It is not possible to show a single instance in which such dumping could be causally linked to a single case of cancer. However, epidemiologists advise that the cancer risk for a million people has been raised, say, 0.1%. Thus, causality is diffusely distributed.

Conversely, categorical thinking also makes it difficult to deal with the situation in which multiple agents caused a single event. Suppose two men start fires simultaneously, at opposite ends of a property. The fires merge and burn down the property. Who is responsible for the damage? Each of the two arsonist defendants can correctly make the same point: if I had not set the fire, the property would still have burned. So how can I be guilty? For much of American history, both would have gone free. It was only in 1927 that the courts declared for the first time that guilt for a singular burning, a singular injury, a singular killing, could be distributed among contributing parties (Kingston versus Chicago and NW Railroad, concerning two fires of different origins that converged). As an implicit acknowledgement of the legal difficulties in dealing with the idea of multiple causes of a single event, if two men, as a pair, are accused of a killing spree, they will readily be tried separately.

As an extension of this, the legal system has no capacity for contingent judgements. Thus, in considering the two accused murderers, suppose one is barely out of adolescence, the two have something resembling a parent–child relationship, with the older of the pair exerting a great deal of persuasive power over the younger one. While the asymmetry of that relationship may be aired in building the defence for the younger man (as is the case in an ongoing trial in the USA), there is no formal charge that can be given to the jury of 'if and only if A, then B': 'the younger man can be found guilty if and only if the older man is first found guilty by a separate jury'.

The early decades of twentieth century medicine were dominated by single causal and single consequence models: a single virus is the sole cause of polio and does nothing but cause polio; a single different virus is the sole cause of yellow fever and does nothing but cause yellow fever, and so on. But now, medicine predominantly deals with multifactorial diseases, such as heart disease, diabetes and cancer, and lifestyle factors that diffusely increase the risk for a multitude of diseases (e.g. smoking, high fat consumption, sedentary lifestyle). The same is true at the levels of systems physiology and cell biology, where functioning involves considerable amounts of convergence and divergence amid various regulatory pathways. Finally, contingent interactions among causal agents are at the heart of how living systems work. Consider genetics, the discipline that the lay public probably (erroneously) considers to be the best example of single agent causality (genes as the holy grail of life, any given gene 'commanding' the cell/organ/body what to do). In actuality, it is nearly meaningless to ever state what a particular gene 'does'. Far more accurately, it is instead the case of genes having a particular effect only in a particular environment (Moore 2002).

Thus, there are enormous intellectual differences between the worlds of science and of law in the basic premises about causality and certainty. With that as an orientation, we now consider how the concept of volition has played a shifting role in thinking about the insanity defence, and what contemporary neuroscience has to offer on this subject.

3. KNOWING RIGHT FROM WRONG: THE GROWING RELIANCE OF THE AMERICAN CRIMINAL JUSTICE SYSTEM ON *M'NAGHTEN*

In the USA, the core of the insanity defence is a derivation of the *M'Naghten* rule from English case law. This well-known test of insanity requires that the perpetrator, because of some mental disease, was unable to understand the nature or quality of the act that he or she performed, or did not know that the act was wrong. As stated in the most commonly understood sense, this insanity defence revolves

around a cognitive disability, namely the inability to know the difference between right and wrong.

The *M'Naghten* rule was criticized on several grounds including, of greatest relevance to this piece, its disregard of mental illnesses that impair volition. Impaired volition has been considered relevant to criminal justice at least beginning with Aristotle (English 1988), and is the idea that it is possible for a person to retain the cognitive capacity to distinguish right from wrong behaviour and, nonetheless, for reasons of mental illness, to be organically incapable of regulating the appropriateness of their behaviour. As a result of this, some states and federal courts expanded upon *M'Naghten* to incorporate the issue of impaired volition. Some rulings introduced throughout the nineteenth century incorporated 'irresistible impulse', a concept that readily proves problematic (i.e. distinguishing between an irresistible impulse and one that is to any extent resistible but which was not resisted). Another test (the American Law Institute Model Penal Code, introduced in 1962) was less absolutist, requiring a 'substantial' rather than complete loss of volition. Another, the *Durham* test, introduced in 1954, stated that a person could be judged innocent by reason of insanity if their criminal act was the 'product' of their mental disease or mental defect (reviewed in Dressler 2001).

By the early 1980s, half the USA and most federal courts were using some sort of insanity test that incorporated elements of loss of volition. This trend abruptly reversed when the potential assassin of Ronald Reagan, John Hinckley, was acquitted on grounds of insanity. This ignited spasms of protests throughout the USA, producing tremendous pressure on courts and legislatures to: (i) narrow the range in which impaired volition could be used as an insanity defence or, more severely; (ii) to retrench back to a sole reliance on *M'Naghten*; or, at the most extreme, (iii) to abandon the insanity defence altogether (Hans 1986). Remarkably, this 'reform' was backed by the American Bar Association, and the American Psychiatric Association (both favouring eliminating impaired volition defences) and the American Medical Association (favouring the complete abandonment of the insanity defence (English 1988)).

This retrenchment was opposed by many legal scholars. In some cases, this was based on constitutional grounds (English 1988), whereas in other instances, the opposition was based on utilitarian thinking: for example, a person with impaired volition who has committed a criminal act is less likely to be rehabilitated if incarcerated in prison than if hospitalized psychiatrically (Arenella 1982). Nonetheless, this retrenchment was widespread throughout the USA. In 1984, the American Congress eliminated impaired volition as an insanity defence at the level of federal courts (the Insanity Defence Reform Act of 1984) and, by 1985, most states within the USA had narrowed or eliminated impaired volitional defences in state courts.

Thus, since that time, the criminal justice system in the USA has been dominated increasingly by a view that an inability to tell right from wrong is the sole basis of an acceptable insanity defence. I will now examine how contemporary neuroscience strongly argues against this trend. Instead, we have come to understand increasingly the organic basis of impaired impulse control.

4. THE PREFRONTAL CORTEX: KNOWING VERSUS CONTROLLING

An appreciation of this emerging knowledge requires an exploration of the functioning of one of the most intriguing parts of the brain, namely the PFC. On a certain metaphorical level, the PFC is the closest thing we possess to a superego. Stated in an only slightly more scientific manner, it is the job of the frontal cortex to bias an individual towards doing the harder, rather than the easier thing (Miller & Cohen 2001). Behaviours that are harder to perform are not necessarily ones that are more correct. However, that is often the case, when 'more correct' is used in a behaviourist sense, rather than in a moralistic one. Thus, doing the 'harder' but 'more correct' behaviour implies a circumstance where a rapid reward is available, but where gratification postponement will yield an even larger reward.

I begin by reviewing the workings of the normal PFC. The role of the PFC in doing the 'harder thing' manifests itself in several domains. One is in the realm of cognition. Memory is not a monolithic process; instead, there is a taxonomy of different types of memory. An important distinction is made between explicit, declarative memory, and implicit, procedural memory. The former involves not only knowledge of facts, but conscious awareness of that knowledge. By contrast, implicit, procedural processes are more automatic and non-conscious. Thus, riding a bicycle, shifting the gears on a car, knitting, can all be procedural tasks, once they are mastered. In effect, these are cases where one's hands know the task better than one's head. But procedural tasks are not merely motoric. Instead, they can also include more cerebral tasks that have become over-learned: remembering one's telephone number, singing the national anthem or reciting the alphabet.

Doing a task through an implicit pathway represents the 'easier' version. When we are forced to override an easier, over-learned implicit pathway and perform a related task in a more novel, declarative way the PFC must be engaged, and the more of an implicit pathway that must be overriden, the more PFC activation is increased (Jaeggi *et al.* 2003). This has been shown in various brain imaging studies. This is particularly the case when the new task represents a reversal of a previously mastered task (i.e. the transition from the well-learned, 'when X, do Y' to the novel 'when X, do not do Y'). The PFC provides the metaphorical cerebral backbone needed to keep the prior, easier task from intruding. And as the new task becomes easier, and thus more automatic, PFC activity subsides, until a new rule is imposed in the task (Simpson *et al.* 2001). As such, experimental lesions of parts of the PFC in laboratory monkeys, or accidental damage to the homologous region in the human PFC, impairs the capacity of the individual to shift behaviour adaptively in response to changing patterns of reward (Baxter *et al.* 2000).

The PFC also plays a key role in 'executive' cognitive function. Executive function can be thought of as the strategic organizing of facts. This can be shown in a particular neuropsychological task in which a subject hears, with minimal warning, a rapidly read list of 16 disparate items that can be bought in a supermarket, and then is asked to recite the list back. Most subjects can recall only a few of the items, at which the list is read repeatedly, with the subject asked to recall the items after each reading. It is only after a few repetitions that one begins to discern that the 16

items fall into various semantic categories: four are hardware items, four are fruits, and so on. And with that, an executive transition occurs, where the memory strategy shifts from simply remembering the sequences of items to remembering them grouped into their categories. Subjects with damage to the PFC fail to hierarchically organize the list into categories. This executive grouping represents the 'harder' (but eventually, more effective) strategy, insofar as a subject must inhibit and step back from the easier strategy of simply trying to recall items in the sequence they were read (Delis *et al.* 1987). Intrinsic in the ability of the PFC to do such executive strategizing is its ability to organize information both sequentially and categorically. Electrophysiological studies of non-human primates have indicated that there are PFC neurons that respond to sequences or to categories of information (Freedman *et al.* 2001; Fujii & Graybiel 2003).

Of great relevance, the PFC role of 'biasing towards doing the harder thing' pertains to emotional regulation as well. For example, in one study, volunteers are shown a film clip of a graphic and disturbing scene: an amputation. In the 'attend' group, subjects are instructed to do what is easiest, which is to simply be aware of the (typically, strong and negative) feelings evoked by the viewing. In the 'reappraisal' group, subjects are instructed to perform the far harder task of regulating those emotions, 'so that they no longer feel negative responses'. And as shown with functional brain imaging during this task, the harder reappraisal task is associated with activation of regions of the PFC (Ochsner *et al.* 2002). Findings strongly in agreement with ones such as these come from studies of individuals with repressive personalities, individuals who are highly self-regulating in their emotional expressiveness. Such individuals have elevated metabolic rates in the PFC (Tomarken & Davidson 1994).

Research has explored a subtler example, perhaps, of doing the harder thing within an emotional realm. In one session, volunteers undergoing functional brain imaging were given a purely cognitive task to think about. In a second imaging session, they would be read a scenario in which someone did an act that might be considered inappropriate; the subject is then told about some unfortunate circumstance in the life of that person that may mitigate the inappropriate act. Regions of the PFC were consistently activated in the latter scenario, one that called forth contemplating empathy and forgiveness (Farrow *et al.* 2001).

Findings such as these lead to a consideration of the role of the PFC in moral reasoning. Several well-designed studies have required subjects to do some manner of moral reasoning (to decide what behaviour they would choose in a morally ambiguous situation) versus reasoning about the physical world (for example, considering whether one object is heavier than another). Consistently, the moral reasoning scenario preferentially activates parts of the PFC (Greene *et al.* 2001; Schultz *et al.* 2001; Heekeren *et al.* 2003; Moll *et al.* 2003). Moreover, making a *decision* in the face of a moral quandary activates more of the PFC than merely contemplating a moral quandary (Moll *et al.* 2002). Another example links the PFC to moral reasoning. Different types of epilepsies originate—have an epileptic 'focus'—in different parts of the brain, and thoughts, sensations or actions just before a seizure reflect the brain region where the seizure commences. For example, an epileptic with a seizure focus in the olfactory cortex might have an olfactory 'aura' just before a seizure. Remarkably, some epileptics whose foci are in the PFC have a pre-seizure cognition of an unresolved moral quandary (Cohen *et al.* 1999).

A recent paper also implicates the PFC in the sensation of regret. In an elegant experimental design, subjects were allowed to participate in a gambling game. In the control scenario, subjects spun a 'wheel of fortune', producing a rewarding or punishing outcome; the latter would typically provoke a sense of disappointment. In the experimental setting, two wheels of fortune were spun, with subjects having chosen to gamble on only one of them. Thus, in that scenario, subjects not only found out if they were punished or rewarded, but also found out what the outcome would have been had they chosen the other wheel. This could result in the particularly aversive situation in which the subject's choice produced a punishing outcome, whereas the other wheel produced a strongly rewarding one. In normal subjects, this resulted in a constellation of affective, behavioural and physiological changes: (i) a subjective sense of regret (of not having picked the other wheel); (ii) a subsequent shift in behaviour towards choosing the other wheel; and (iii) pronounced arousal of the sympathetic nervous system. By contrast, in a group of patients with extensive damage to the PFC, none of the responses occurred (Camille *et al.* 2004).

Most importantly, the PFC mediates doing the harder thing in the realm of behaviour as well. Stated in terms most pertinent to this essay, the PFC helps to suppress impulsive behaviour. As will be discussed below, this has been amply documented in humans with PFC damage, who fail to carry out the harder, less impulsive behaviour. This can be shown more formally with laboratory rats; upon completing a task such as lever pressing, they can either get a reward (typically food) after some delay, or can opt to get a lesser reward but with no delay. In some testing paradigms, up to 90% of rats can demonstrate 'gratification postponement', in enduring the long delay for the larger reward. However, if the PFC (or some of the sites that project to it, which will be discussed shortly) is lesioned, the rat consistently opts for the more impulsive choice, amid still retaining the cognitive capacity to perform the task (cf. Cardinal *et al.* 2001).

How does the PFC mediate doing the 'harder' thing? One way to gain insight into this is to review the parts of the brain to which the PFC sends projections. Of greatest relevance to the notion of the PFC controlling impulsivity, the structure sends large inhibitory projections into the limbic system, particularly the amgydala, a region heavily implicated in aggressive behaviour. Strikingly, in humans, elevated metabolic rates in parts of the PFC predict low rates of amygdaloid activity (Urry *et al.* 2003). This neuroanatomy is important in trying to understand the biology of violence. There can be striking similarities in the motor output and the associated physiology (i.e. the actual behaviour, the accompanying changes in heart rate, blood pressure, and so on) when a sniper picks off enemy soldiers and when a sniper randomly picks off motorists driving the evening commute. However, one circumstance earns medals and societal acclaim, and the other the death penalty. The limbic system can function in roughly similar ways in both settings. As societies, we do not outlaw violent acts; we outlaw

them in the wrong context, and the PFC is centrally involved in learning and imposing context.

The PFC also sends projections to much of the rest of the cortex, and to regions of the brain that initiate movements and behaviour. In this realm, many of those projections are stimulatory. However, those excitatory inputs should not be thought as 'activating' (i.e. in a highly schematic sense, 'causing' a thought to arise in the cortex, or 'causing' an action to arise from these motor pathways). Instead, the excitatory inputs are meant to bias one particular output to occur over another. As a very artificial example, insofar as counting from June forwards to December is the overlearned sequence for reciting the months, the pathway that mediates that sequence is intrinsically a stronger one—has more robust synaptic connections—than the pathway that counts from June backwards to January. Thus, when one is called upon to do the harder reversal task, the 'work' that is required from the PFC takes the form of priming that weaker 'June backwards' pathway sufficiently to tilt the balance in its favour over the overlearned, implicit 'June forwards' route (Miller & Cohen 2001).

Further insights into how the PFC mediates doing the 'harder' thing also come from considering the projections to the structure. Appropriately, the PFC receives information from sites throughout the rest of the cortex, including not only sensory processing regions, but more upstream, associative parts as well. Intriguingly, there are also extensive projections into the PFC from parts of the limbic system, the part of the mammalian brain involved in emotion. Such connections probably go far to explain why strong emotions can adversely impact the quality of executive function, often increasing the likelihood of imprudent or impulsive choices.

Arguably, the most interesting projection into the PFC is a pathway originating in the ventral tegmentum and coursing through the nucleus accumbens before continuing on to the PFC (among other regions). This projection has long been known to be involved in mediating pleasure and reward, being a robust site of 'self-stimulation' (i.e. where rats will work, often to extraordinary extents, to be stimulated in this pathway). Central to this role is the fact that this projection uses the neurotransmitter dopamine, which has long been implicated in pleasure and reward. For example, euphoriant drugs such as cocaine enhance dopamine signalling.

Initially, there was the expectation that this dopaminergic projection would cause the PFC to become active in response to reward. For example, consider a task where a trained monkey would be (i) given a signal (e.g. a light) indicating the beginning of a testing session for a task that it has mastered; this would be followed by (ii), the monkey completing the task, thereby initiating a latency until (iii) delivery of the reward. In a paradigm such as this, dopaminergic neurons themselves would be heavily responsive to period (iii), as would some neurons in the PFC. However, unique to the PFC, there would be substantial numbers of neurons responding instead to periods (i) and (ii) (Schultz *et al.* 2000). Thus, critically, dopamine–PFC interactions are not so much about reward as about the *anticipation* of reward.

The PFC can be quite subtle in this anticipatory function. For example, in one study, rhesus monkeys were trained to perform two different tasks. In both cases, there would be an initial stimulus signalling the start of the task. The monkey would then carry out the task, followed by a signal indicating if the monkey's response was correct. In only one of those two tasks, however, was that 'correct' signal then followed by a food reward. PFC neurons were identified electrophysiologically that would distinguish between anticipating feedback indicating a correct action, and feedback indicating a correct action coupled with a food reward (Matsumoto *et al.* 2003).

The activation of the PFC in anticipation of reward is at the core of its function. Like any other pathway in the nervous system, the strength of the dopaminergic projection into the PFC can change. Such plasticity could take the form of an enhanced capacity to sustain dopamine release as the interval between the onset of a task and its reward increases. This would constitute the neural basis of an increasing capacity for self-discipline and gratification postponement.

5. THE HUMAN PREFRONTAL CORTEX AND ITS IMPAIRMENTS

This very broad (and simplistic) overview of PFC function allows us to appreciate circumstances in which PFC function is compromised in a human. Humans comprise a special case when considering this brain region. Despite evidence that the PFC in rodents and non-human primates regulates cognition and behaviour in ways quite similar to that of the human, we are the most 'frontal' of species, insofar as the frontal cortex is its largest, in both absolute and relative terms, in the human (Rilling & Insel 1999).

The first realm to consider where PFC function is compromised in humans is, quite reasonably, during development. Children show only minimal frontal function, from the standpoints of cognition (for example, in reversal tasks), emotional regulation, control of impulsive behaviour and moral reasoning. One of the myths of child development is that the brain is fully developed at some remarkably early age (the age of 3 years is probably most often cited (Bruer 1999)). Instead, brain development is far more prolonged and, not surprisingly, the PFC is the last region of the brain to fully myelinate. Remarkably, this process extends well beyond adolescence into early adulthood (Paus *et al.* 1999).

Various transient states can compromise PFC function. Alcohol is long-recognized for its capacity to impair reasoning and impulse control, and surprisingly small quantities of alcohol impair the capacity of the PFC to detect errors of commission or omission, as assessed electrophysiologically (Ridderinkhof *et al.* 2002). Another example concerns stress. Most individuals have experienced severe and/or prolonged stress as disrupting attention, judgement and other purviews of the PFC, and this has been shown more formally in both humans and animals (Arnsten 2000; Sapolsky 2004). In making sense of this, it should be appreciated that the PFC contains some of the highest levels of receptors in the primate brain for stress hormones (Sanchez *et al.* 2000). Moreover, stress or stress hormones will dramatically alter the turnover of several classes of neurotransmitters in the PFC (Moghaddam *et al.* 1994; Arnsten 2000).

PFC function is also compromised in another circumstance experienced by all individuals. With the onset of

sleep and the transition to deep, slow wave sleep, there is a characteristic decrease in activity throughout the brain, particularly in the cortex. However, with the transition to paradoxical rapid eye movement sleep, there is increased activity in a variety of brain regions, including associational cortex and limbic systems; strikingly, metabolic rate can even be higher than during wake periods. Amid this shift, there is a virtually complete cessation of activity in the PFC, producing a relatively metabolically active brain that is unconstrained by the regulatory effects of the PFC (Braun *et al.* 1998). It has been speculated that this, in effect, accounts for why dreams are 'dream-like': characterized by emotional lability, non-sequential thinking and extreme disinhibition (Sapolsky 2001).

PFC function is also often impaired during normative ageing. There is often the misconception that brain ageing involves massive loss of neurons; this mistake is a result of some early and influential studies in which diseases of ageing (specifically dementias) were not viewed as distinct from normal ageing. In actuality, there is only really one brain region in which there is loss of most neurons during normal ageing (the substantia nigra), and only a few additional regions in which there is even moderate neuron loss. The PFC is among these and, commensurate with that, normal ageing involves a mild degree of impairment of frontal function in several realms (Coleman & Flood 1987; Coffey *et al.* 1992; Tisserand & Jolles 2003).

We now consider the realm of PFC dysfunction most relevant to legal matters, namely, when the frontal cortex is damaged. This literature originates with Phinneas Gage, a man who is arguably the most famous patient in the history of neuropsychology. Gage's PFC was selectively destroyed in an industrial accident some 155 years ago, and it transformed him, virtually overnight, from a taciturn, reliable foreman in a railroad construction crew to a coarse, disinhibited unstable individual who was never able to work again (MacMillan 2000). Since then, an extensive literature links PFC damage with impulse control, antisocial behaviour and criminality (reviewed in Brower & Price 2001; Nyffeler & Regard 2001), as well as more quantifiably 'frontally disinhibited' cognition and behaviour in the context of more formal testing.

There is an increasing appreciation that the age at which the PFC damage occurs can be critical (Damasio 1998; Brower & Price 2001; Moll *et al.* 2003). The general picture is that damage any time after the adolescent years produces an adult who is markedly impulsive in behaviour, and with little capacity for foresight or assessing future consequences when in an emotionally aroused circumstance. Amid that, general intelligence and executive function can remain intact. By contrast, when damage occurs at earlier ages, executive function is impaired and the impulsivity takes on a more global and malign nature that has been termed 'acquired sociopathy', where antisocial behaviours can be markedly premeditated.

The issue of brain development becomes relevant when considering individuals with sociopathic and antisocial behaviour in which there is no obvious history of PFC damage. Despite there being nothing demonstrably, neurologically 'wrong' with such individuals, an abundant literature demonstrates that their PFC, nonetheless, works somewhat differently than most other individuals. Thus, basal metabolic rates in the PFC are decreased in sociopaths (Raine 2002). Moreover, when sociopaths must engage the PFC (i.e. during neuropsychological testing when they are attempting to successfully perform a frontally demanding task), they activate more of the PFC than control individuals to achieve the same level of efficacy (Abbott 2001). In other words, even when these individuals actively attempt to do the 'harder thing', their PFCs are less effective. Importantly, among such sociopathic individuals, the smaller the volume of the PFC (where, again, there is no history of overt PFC damage), the greater the tendency towards aggressive and antisocial behaviour (reviewed in Brower & Price 2001).

Probably the most common cause of major PFC damage in humans is secondary to a stroke. Such 'ischaemic' damage produces an individual who can be highly impaired in cognitive tests of frontal function, and behaviourally and affectively disinhibited (Lezak 1995). The same is seen with fronto-temporal/Pick's dementia, a rare neurodegenerative disorder in which neuron loss is initially concentrated in the PFC (Chow *et al.* 2002). Because strokes and such dementias are situations in which a previously cognitively intact adult loses cortical function (as opposed to the situation of, say, the 3-year-old who has not yet developed full frontal function), this can provide one of the most extraordinary features of PFC damage. During neuropsychological testing, the patient might say, in effect, 'I know, I know how this test works, I am supposed to choose this trickier one because it gets me more of a reward, so that is just what I am going to. . .' before impulsively taking the 'easier' route (Lezak 1995). Thus, the frontally damaged patient can verbalize the dissociation between knowing the right from wrong response, and being able to act upon that knowledge.

6. SOME CONCLUSIONS: THE FRONTAL CORTEX AND THE CRIMINAL JUSTICE SYSTEM

We have come to recognize numerous realms in which a biological abnormality gives rise to aberrant behaviour. And such recognition has often then given rise to an expectation that people now exert higher-order control over that abnormality. For example, as noted, we would never consider an epileptic violent who strikes someone in the process of a seizure: 'it is not him; it is his disease'. However, we expect that epileptic to not drive a car if their seizures are uncontrolled. Or we are coming to understand the neurochemistry of context-dependence relapse into drug dependency in organisms. Thus, we have come to expect ex-addicts to avoid the settings in which they previously abused drugs.

There is a false dichotomy in this manner of thinking. It is as if we artificially demarcate an area in which biology dominates: yes, there is something organic that gives rise to this person having uncontrolled and synchronous neuronal discharges (i.e. a seizure), or who has certain pathways potentiated that project onto dopamine-releasing 'pleasure' pathways (one theory about the neurochemistry of substance abuse relapse). But it is as if, with that area of organic impairment identified and given credence, we expect it to be bounded, and for the rest of our 'us-ness', replete with free will, to now shoulder the responsibility of keeping that organic impairment within the confines of its boundaries. It cannot possibly work this way. What the

literature about the PFC shows is that there is a reductive, materialistic neurobiology to the containment, resulting in the potential for volitional control to be impaired just as unambiguously as any other aspect of brain function. It is possible to know the difference between right and wrong but, for reasons of organic impairment, to not be able to do the right thing.

The most obvious implication of this concerns how individuals with demonstrable PFC damage are treated in the criminal justice system. As the simplest conclusion, everything about this realm of contemporary neurobiology argues against the retrenchment back towards a sole reliance on *M'Naghten* that has gone on in recent decades.

Amid the seeming obviousness of this conclusion, there is always a valid counter-point that can be raised: there are individuals with substantial amounts of PFC damage who, nonetheless, do not commit crimes. At present, knowing that someone has sustained PFC damage does not give much power in predicting whether that person's disinhibition will take the form of serial murder or merely being unable to praise a nearly inedible meal prepared by a host. This seems to weaken the 'volition can be organically impaired, just like any other aspect of brain function' argument; in these interstices of unpredictability seem to dwell free will.

However, we can begin to imagine tree diagrams of variables that, with each new layer, add more predictive power. We can already see two layers in the realm of PFC function. The first layer might query, 'PFC: normal or damaged?' (while recognizing that this is a false dichotomy). The second might then query, 'if damaged: damaged in childhood or later?' This same structure of increasing predictive power was shown in a recent, landmark study concerning clinical depression. Having a particular variant of the gene 5-HTT (which codes for a protein that regulates synaptic levels of the neurotransmitter serotonin) increases the risk of depression. However, '5-HTT: pro-depressive variant or other variant?' gives only a moderate predictive power, but the authors then demonstrated the adding in of a second layer, 'if the pro-depressive variant: major stressors during childhood or not?' now generates an impressive predictive power as to which adults succumb to clinical depression (Caspi *et al.* 2003). If free will lurks in those interstices, those crawl spaces are certainly shrinking.

A second way in which findings about the PFC are relevant to the criminal justice system concerns individuals who have committed grotesquely violent, sociopathic crimes, but who have no demonstrable PFC damage. Initially, it seems a fatuous tautology to say that there must be an organic abnormality in such cases—'it is only an organically abnormal brain that produces abnormal behaviour'—and that we simply lack sufficiently sensitive techniques for demonstrating it. However, it must be emphasized that most of the neurobiological techniques used to demonstrate PFC abnormalities in humans (predominantly structural and functional brain imaging) did not exist a decade or two ago. It would be the height of hubris to think that we have already learned how to detect the most subtle ways in which PFC damage impairs volitional control. Instead, we probably cannot even imagine yet the ways in which biology can go awry and impair the sorts of volitional control that helps define who we are.

At the most disturbing level, findings about the PFC are relevant to the criminal justice system with respect to those of us with a normal PFC and who have never behaved criminally. It is here that the tendency of science to function in continua comes up against the legal culture of jury decisions. Among sociopaths without overt PFC damage, the smaller the volume of the PFC, the greater the tendency towards aggressive and antisocial behaviour (reviewed in Brower & Price 2001). Similarly, as noted, among humans with no neurological impairments or histories of antisocial behaviour, the greater the level of metabolic activity in parts of the PFC, the lower the activity of the amygdala (Urry *et al.* 2003). There is little support for the idea that over the range of PFC function, there is a discontinuity, a transition that allows one to dichotomize between a healthy PFC in an individual expected to have a complete capacity to regulate behaviour, and a damaged PFC in someone who cannot regulate their behaviour. The dichotomy does not exist.

A conclusion like this makes sense to neurobiologists, but may seem alien to legal scholars. The emphasis on continua seems to hold the danger of a world of criminal justice in which there is no blame and only prior causes. Whereas it is true that, at a logical extreme, a neurobiological framework may indeed eliminate blame, it does not eliminate the need for forceful intervention in the face of violence or antisocial behaviour. To understand is not to forgive or to do nothing; whereas you do not ponder whether to forgive a car that, because of problems with its brakes, has injured someone, you nevertheless protect society from it.

Legal scholars have objected to this type of thinking for a related reason, as well. In this view, it is desirable for a criminal justice system to operate with a presumption of responsibility because, 'to treat persons otherwise is to treat them as less than human' (Morse 1976). There is a certain appealing purity to this. But although it may seem dehumanizing to medicalize people into being broken cars, it can still be vastly more humane than moralizing them into being sinners.

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GLOSSARY

PFC: prefrontal cortex