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The neurobiology of antisocial personality disorder: The quest for rehabilitation and treatment☆

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ABSTRACT

Psychopathy is perhaps one of the most misused terms in the American public, which is in no small part due to our obsession with those who have no conscience, and our boldness to try and profile others with this disorder. Here, I present how psychopathy is seen today, before discussing the classification of psychopathy. I also explore the neurological differences in the brains of those with psychopathy, before finally taking a look at genetic risk factors. I conclude by raising some questions about potential treatment.

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1. Introduction

Psychopaths remain a strong component of popular culture. Despite inflicting terror into our hearts with the idea of a remorseless killer who is "programmed" to kill, they are also heralded as intrinsically fascinating. The television show *Dexter*, based on the series of novels by Jeff Lindsay, even deifies the psychopath; although the main character has been instilled with a code that only allows him to murder the most despicable of criminals. The idea of satisfying the *dark passenger* with sacrifices of murderers and rapists seems to be morally permissible to many. Although, despite the apparent indifference to extreme violence, perhaps the most frightening fact about psychopaths or those with extreme Antisocial Personality Disorder (APD), is that there currently does not seem to be a cure, clinical or pharmacological; this rules out any real chance at a successful rehabilitation.

Innovations in brain science have also kept the psychopath in the spotlight. Breakthroughs in fMRI analysis have re-opened debates concerning morality and the regions of the brain that are used in our so-called moral decisions. In his timely and fascinating book *The Science of Evil*, Simon Baron-Cohen lists the components of what he calls *The Empathy Circuit*, the brain areas that are utilized during

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acts of empathy.[1] This list of 13 regions includes the amygdala, the caudal anterior cingulate cortex, the medial prefrontal cortex (dorsal and ventral), the orbitofrontal cortex, and the middle cingulate cortex (Baron-Cohen, 2011). These regions will be discussed later in light of APD, as well as some contemporary research that looks for a genetic explanation of the disorder.

1.1. Classifying APD and psychopathy

The task of classifying APD has been arduous, mainly because the disorder seems to be responsible for a range of extreme behaviors. In 1941, Cleckley listed 16 criteria for psychopathy in his book *The Mask of Sanity*, the most pertinent ones perhaps being *superficial charm and intelligence*, *lack of remorse or shame*, *sex life impersonal, trivial, and poorly integrated* (Ogloff, 2006). Today, the DSM-IV has divided personality disorders into clusters (due to common characteristics of each); APD is listed in the dramatic–eccentric–emotional cluster, which also includes Borderline Personality Disorder, Histrionic Personality Disorder, and Narcissistic Personality Disorder (Ogloff, 2006). This cluster of disorders, with the exception of Histrionic Disorder, as also tied together by Baron-Cohen as disorders that result in *zero degrees of empathy*; zero degrees of empathy for Baron-Cohen means that those afflicted "have no awareness of how [they] come across to others, how to interact with others, or how to anticipate their feelings or reactions. [Their]Empathy Mechanism functions at Level 0" (Baron-Cohen, 2011). Due to these significant deficits, successful and continued social interactions are difficult to maintain, and the response of others to those with these disorders, especially during extreme bouts of uninhibited maladaptive behavior, will no doubt be negative.

The best quotient for determining psychopathy, however, seems to be the Psychopathy Checklist devised by Hare in the 1980s; this is what separates the psychopathic from the non-psychopathic of those with APD. This checklist was revised in 1991, and a version for adolescents and children was also constructed about a decade later (Blair, Blair, & Mitchell, 2010). The revised checklist for adults is scored out of 40 and anyone scoring over 30 is considered psychopathic (Blair et al., 2010).

The job of classifying APD and psychopathy is conducted purely on a behavioral basis; the behavior of certain individuals is witnessed and discussed by mental health experts, and with the use of various analytical methods the afflicted individual is diagnosed. However, there are significant differences in brain areas of those with APD, and contemporary methods of brain scanning have helped to elucidate many of these. There is also a distinction between "successful" and "unsuccessful" psychopaths based upon their history of incarceration (unsuccessful psychopaths are incarcerated frequently and vice-versa). Perhaps unsurprisingly, successful and unsuccessful psychopaths also show significant differences in brain development; some of these will be explained later.

The developmental differences in those with APD appear to be the result of lifestyle and nurturing in the formative years. However, some studies have also indicated a genetic significance, suggesting that there could be a genetic predisposition for the onset of APD. With a greater understanding of the conditions, both environmental and biological, which lead to these neural differences, it might be possible to devise an effective method of treatment.

1.2. Neurological basis for aggression and operant conditioning

Before assessing the neurological deficits in those with APD, it is important to consider the circuitry involved in aggression and reward-based learning. Aggression is typically divided into two categories; reactive aggression (reacting to a threat), and instrumental (using aggression for personal goals). The neural threat system is said to include the amygdala, the hypothalamus, and the dorsal half of the periaqueductal gray (PAG) (Gregg & Siegel, 2001). Blair (2004) has suggested that this circuitry is regulated by regions of the frontal cortex, such as the orbital, medial, and ventrolateral frontal cortices. If the frontal lobe exerts executive control over this threat circuitry, it could mean that deficits in the frontal lobe impair threat-response regulation and even hinder the function of additional regions, increasing the likelihood of unforeseen and potentially problematic behavior; although as Blair speculated, clearly more research needs to be done.

The threat circuitry mentioned above is implemented in reactive aggression; the greater the activity in this circuit, the greater the chances for reactive aggression (Blair, 2010). Reactive aggression is a primal response to an immediate threat; the body conveniently prepares for these responses by activating the sympathetic nervous system and increasing activity in the hypothalamus (part of the threat circuitry); this typically results in increased awareness and heightened blood pressure. Psychopaths, however, appear to show deficits in this type of response. According to Blair, psychopaths are typically impaired on tasks that rely on a functional amygdala — these include aversive conditioning, passive avoidance learning, augmentation of the startle reflex by threatening visual primes, and fearful face recognition (Blair, 2010). With a reduced capacity for both aversive conditioning and passive avoidance learning, the psychopath is denied crucial forms of emotional learning which no doubt contributes to their lack of empathy because they are unable to tag memories and experiences with emotional salience.

1.3. Neurological impairments in those with APD

Raine, Lencz, Birhle, LaCasse, and Colletti (2000) wanted to see if those diagnosed with APD shared the same prefrontal deficits as those suffering from "pseudopsychopathic" disorder[2]; in fact, this has been termed "acquired sociopathy" and has been linked to damage inflicted to the orbitofrontal cortex (Damasio, 1998). Of the APD group used by Raine and his team, 52.4% of them reported having assaulted a stranger, 42.9% of them were guilty of rape, 38.1% were guilty of firing a gun at someone, and 28.6% of them were guilty of attempted or completed homicide. Using magnetic resonance imaging (MRI), Raine et al. (2000) found that prefrontal gray matter was reduced by about 11% in comparison to the control group. This represents a substantial absence in gray matter in the prefrontal regions of those with APD,[3] and indicates that a serious developmental abnormality must have occurred to prevent these areas from growing.

Deficits in frontal gray matter were also correlated with a reduction in autonomic function. Raine et al. (2000) divided the APD group along the median value for gray matter volume into a "high" prefrontal gray group and a "low" prefrontal gray group. They found that the low prefrontal gray group had a reduction in galvanic skin response when discussing their antisocial (and often criminal) behavior; there was no difference in heart rate, however. With the absence of such a significant portion of gray matter in the frontal lobe, one can only wonder at other functional deficits that could be present, especially in executive functioning and working memory.

In a later study, Yang, Raine, Colletti, Toga, and Narr (2010) used MRI and found statistically significant deficits in gray matter volumes of

[1] Empathy appears to be the crux that enables science to stake a claim in moral philosophy.

[2] These patients have suffered neurological damage to the frontal lobes from injury and exhibited APD traits.

[3] Raine et al. (2000) state that the prefrontal regions include "all of the cortex anterior to the genu of the corpus callosum, and was divided into the left and right hemispheres along the longitudinal fissure."

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unsuccessful psychopaths when compared to the control group in three different regions; the right middle frontal cortex, the left and right orbitofrontal cortices, and the right gyrus rectus. The authors of the study go on to speculate that deficits of gray matter in these regions predispose unsuccessful psychopaths to impulsive and risky behavior and oblivious to cues that could signal arrest. A remarkable facet of this study, however, shows that there is no significant difference between volumes of gray matter between successful psychopaths and the control group. Having no deficits in gray matter in the frontal lobe suggests that successful psychopaths have a higher degree of executive functioning and perhaps even a predisposition for increased working memory[4] over their unsuccessful counterparts. This also raises the question of whether successful psychopaths have any deficits and where they could be located.

Significant reductions in both the left and right amygdala were also noted in unsuccessful psychopaths in comparison to the control group (Yang et al., 2010). Deficits in the amygdala seem to bolster the notion that psychopaths are impaired when it comes to tasks that involve the amygdala, as mentioned earlier. However, in successful psychopaths, even though they showed a slight reduction in amygdala volume in comparison to the control group, the difference was not statistically significant.

The orbitofrontal cortex and the amygdala are joined by a tract (a bundle of myelinated nerves in the CNS) by the Uncinate Fasciculus (UF). This tract was examined by Craig et al. (2009) to see if the structural integrity differed in psychopaths when compared to a healthy control group. If the frontal lobe and the amygdala are implicated in psychopathy, it is not unreasonable to assume that the tract allowing communication between the two regions could also show some developmental defects. Using diffusor tensor magnetic resonance imaging tractography (DT-MRI),[5] Craig et al. (2009) were able to study the white matter tracts in those with psychopathy and determine the integrity by looking at the number of streamlines (SL) and by measuring the mean fractional anisotropy (FA), which is an indirect measure of white matter structure. Streamlines are a physical measure of tract volume, whereas FA is a measure of structural integrity; because it is thought that the extent and quality of myelination in a tract should prevent the random diffusion of water molecules at its best (an FA value of 1), compared to a poorly insulated and degraded tract that will show an FA value closer to zero. Craig et al. (2009) found that the right UF had a significantly lower FA than the left in psychopaths when compared to the healthy control group, whereas the number of SLs was not significant between the two groups.[6]

According to Craig et al. (2009), degradation of the UF is also associated with Kluver–Bucy syndrome (a syndrome showing increased aggression and loss of fear response). Children with reduced UF integrity show impulsive traits and a lack of socio-emotional integration, and it is also present in those with Borderline Personality Disorder.

Abnormalities have also been found in the symmetry of the hippocampi in unsuccessful psychopaths. Raine et al. (2004) found that unsuccessful psychopaths have an exaggerated asymmetry in the anterior hippocampus (right bigger than left), when compared to the healthy control group. An interesting point raised by Raine et al. (2004) is that an exaggerated asymmetry between right/left hippocampi is normally present in the fetus and becomes less exaggerated during the normal development of the child; thus, this normal development could be blocked or hindered as the child develops a personality disorder. Broken homes and uncaring families have long been implicated in the environmental conditions surrounding critical developmental periods in children with conduct disorder (CD)[7] (Farrington, 2005). A traumatic upbringing could also be implicated in the deficits found in all of the aforementioned brain regions. Apart from being involved in the threat circuitry, the hippocampus is also implicated in spatial memory. If unsuccessful psychopaths suffer from poor memory, it could contribute to their inability to make good cognitive judgments. Memory deficits and poor social conditioning no doubt lead to poor integration.

There appears to be a dynamic neural system (that is no doubt contingent upon input from other regions) between the frontal cortex and the limbic regions. Deficits in the frontal cortex (particularly the orbito frontal region), deficits in the amygdala, and deficits in the tract that joins the two, seem to be implicated in personality disorders or syndromes that involve aggression and social integration. The damage to these regions no doubt has behavioral implications for other regions that communicate with them via efferent/afferent tracts, such as the threat system involving the amygdala,[8] hippocampus, and PAG, and higher order executive functions involving the frontal cortices. At the moment there are limited studies on these second-order implications outside of this immediate neural region.

Neuro-developmental abnormalities in the corpus callosum have also been implicated in APD. Raine et al. (2003) discovered that the corpus callosum in those with APD is about 22.6% larger in volume than control group; however, no distinction was drawn between unsuccessful and successful psychopaths. The corpus callosum is a region in the brain composed largely of white matter that allows a high degree of communication between the two hemispheres of the brain. Raine et al. (2003) suggest that this increase in white matter could be the result of maldevelopment between the left and right hemispheres because as much as two-thirds of the corpus callosum is "pruned" during early childhood. If the corpus callosum does not reduce after childhood, therefore, the important steps resulting in the shaping of the corpus callosum have been hindered or eliminated.

1.4. A genetic look at those with APD/psychopathy

Identifying genetic factors involved in antisocial personality disorder appears more difficult than identifying structural abnormalities; the identification of genetic abnormalities in an organ composed of over a billion neurons with over a trillion synapses makes looking for a needle in a haystack seem like child's play. Nevertheless, certain genes have been identified in personality disorders, and like structural abnormalities, they appear to be involved in a number of similar disorders. For example, the gene C-521T, which is involved in the creation of the dopamine 4 receptor, has been implicated in novelty-seeking and impulsivity (Basoglu et al., 2011); numerous personality disorders, including APD, exhibit this trait.

Basoglu et al. (2011) also found that SNAP 25, a protein located on the presynaptic membrane that is involved in the docking of synaptic vesicles on the membrane, is also implicated in APD. SNAP 25 polymorphisms (MnII T/T and Ddel T/T alleles) have also been implicated in ADHD and Schizophrenia, as well as in APD; the MnII T/T and Ddel T/T alleles for this protein were higher in those with APD than in a sex-matched control group (Basoglu et al., 2011). Basoglu et al. (2011) hypothesize that the SNAP 25 protein, which plays a role in exocytosis, could fundamentally alter neurotransmitter systems, causing profound changes in the brain. The authors also point out that all of the cluster B personality disorders in the DSM IV seem to display a behavior that could be a result of SNAP 25 polymorphisms. Perhaps future versions of the DSM or a complementary manual will list genetic

[4] Working memory has long been associated with frontal lobe activity (Prabhakaran, Narayanan, Zhao, & Gabrieli, 2000).

[5] DT-MRI appears to be vastly superior to the MRI seeding program that Raine et al. (2000) used to determine water matter volume.

[6] Craig et al. (2009) also controlled for substance abuse and still found that the differences in FA of the UF were unique to the psychopath group alone.

[7] Conduct Disorder is a personality disorder reserved for children and adolescents who show antisocial traits.

[8] The amygdala also communicates with the superior temporal sulcus, the fusiform cortex, and the anterior cingulate cortex (Blair, 2010).

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equations that help diagnose personality disorders, rather than just relying on behavior analysis?

A genetic abnormality of the Monoamine Oxidase A (MAO-A) gene has also been linked to antisocial behavior. This gene is located on the X chromosome[9] and a rare mutation of this gene, which has not been identified in the population at large, was identified in a Dutch family where many of the men exhibited extreme antisocial behaviors, including rape and assault (Merriman & Cameron, 2007; Raine, 2006). This gene produces an enzyme (MAO) that breaks down monoamine neurotransmitters such as dopamine and serotonin; a defunct MAO enzyme would result in elevated levels of these neurotransmitters, and this has been correlated with aggressive behavior (Merriman & Cameron, 2007).

There have also been correlations drawn between MAO activity and the severity of the maltreatment of children (Caspi et al., 2002). Caspi et al. (2002) found that low MAO-A activity in children who had been seriously abused seemed to result in high probability of having CD, had an inordinate predilection for violent behavior, and were more likely to be convicted of violent offenses than children who were not abused and also had low MAO-A activity. This study is very important, because it appears to shed some light on environment/gene interactions, i.e. physical abuse directed at a child with low MAO activity increases the likelihood of antisocial behavior, even though about 20% of the sample of children who suffered no abuse and had low MAO activity still exhibited CD.

2. Conclusion

From looking at the development defects in those with antisocial personality disorder (from functional integrity of brain regions to genes and neurotransmitters), it is not difficult to see why classifying APD has been a difficult and arduous task. There appears to be no one causal factor for the disorder. And many of the dysfunctions that are evident in those with APD are also prevalent in other disorders (even though many of these do seem to be grouped together in various diagnostic manuals). Further, not only does APD share neurological similarities with other disorders, there is also a significant variance in those with APD, notably those classified as successful and unsuccessful psychopaths.[10]

Due to the sheer complexity of factors behind APD, it is hard to imagine how a treatment program, either pharmacological or clinical, could be devised to help those afflicted to overcome this disorder. Defective or mal-developed brain regions could very well be the result of serious childhood abuse, and so the most effective preventative measure could be to tackle childhood abuse. Once the brain has stopped developing, these neurological impairments could very well be permanent because the developmental pathways cease once they are cued to finish at a certain age. It is currently hard to imagine using neural stem cells to repair deficits in gray and white matter in those with APD, because developmental errors will have caused such profound changes in the brain over time that an adequate treatment plan would be impossible.

A second problem in treating those with APD is that none of those afflicted are going to openly volunteer for any treatment plan; they have a limited conscience and capacity for empathy, and do not believe there is anything wrong with them. This means that there will only ever be two paths for treatment of this disorder. The first is refining techniques to predict the onset of this disorder and develop methods to counteract it. The second would be to develop a treatment for those with these neurological impairments that would have to be forced upon them; this could be done with unsuccessful psychopaths, perhaps as a condition of parole. However, how would you convince successful psychopaths to voluntarily take it, even if it existed? Clearly, the more we can understand about this dangerous personality disorder, the better.

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[9] As this is an x-linked trait and the trait only seemed to be exhibited in men, it appears to be an x-linked recessive trait. If the women had a normal MAOB gene on their other X chromosome, they are merely destined to carry it rather than exhibit the deleterious effects of the mutant gene.

[10] To my knowledge there has been no genetic study that has explored differences between successful and unsuccessful psychopaths.

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