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Cognition to genes via the brain in the study of conduct disorder

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Cognition to genes via the brain in the study of conduct disorder

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Although a single diagnostic label, conduct disorder, is currently applied to children exhibiting anti-social behaviour, multiple routes to the same behavioural phenomena exist. Morton and Frith's (1995) causal modelling has been fundamentally important in influencing models of cognitive/affective and associated neural differences between callous-unemotional (CU) and reactive/threat-based antisocial behaviour. Current behavioural genetic research is still catching up with the developmental cognitive neuroscience, and very few genetically informative studies differentiate between these two subtypes of antisocial behaviour. Our own work with preadolescent twins suggests that while the CU subtype is genetically vulnerable to antisocial behaviour, the non-CU subtype manifests a primarily environmental aetiology to their antisocial behaviour. Molecular genetic work to date has not differentiated between these two subtypes, and we highlight why it might be of interest to do so. Finally, we discuss how the novel approach of imaging genetics could be harnessed to study genes to cognition pathways for different subtypes of conduct disorder. Uta Frith's contributions to articulating research strategies for developmental disorders are important in conducting and interpreting this work.

Preventing antisocial behaviour and violence is one of the most important global concerns and also features as a UK National Health Service and Government research priority (Bailey, 2002; Krug, Dahlberg, Mercy, Zwi, & Lozano, 2002). Political, social, and economic risk factors for antisocial behaviour are well studied (Farrington, 2000). In addition a growing number of studies

attest to genetically influenced individual differences in predisposition to antisocial behaviour and violence (Moffitt, 2005; Rhee & Waldman, 2002). We use the terms antisocial behaviour, conduct disorder, and conduct problems interchangeably in this paper to refer to the violation of social norms and rights of others, rather than as a clinical label.

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Early-onset antisocial behaviour carries a strong risk for persistent offending (Moffitt, 2003). In childhood, high levels of antisocial behaviour may be diagnosed as conduct disorder (CD). The *Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition* (DSM-IV; American Psychiatric Association, 1994) defines CD as persistent antisocial behaviour, which deviates from age-appropriate social norms and violates the basic rights of others. The prevalence of CD in the UK is 2.1% for boys and 1% for girls, and the risk of being diagnosed increases with age (Maughan, Rowe, Messer, Goodman, & Meltzer, 2004).

Although a single diagnostic label, conduct disorder, is currently applied to children exhibiting antisocial behaviour, multiple routes to the same behavioural phenomena exist. This point has been illustrated several times over and with regard to various developmental disorders by Uta Frith and her colleagues (Blair & Frith, 2000; Frith & Happé, 1998; Morton & Frith, 1995). One way of subtyping conduct-disordered children is to highlight the cognitive/affective differences between callous-unemotional (CU)/premeditated and reactive/threat-based antisocial behaviour (Blair, Peschardt, Budhani, Mitchell, & Pine, 2006; Frick et al., 2003; Pardini, Lochman, & Frick, 2003). In this paper we present data that suggest that the extreme behaviour seen in CU and non-CU antisocial individuals (from now on AB/CU+ and AB/CU–, respectively) is likely to stem from different types of deficits at the cognitive-affective level, probably reflecting the operation of differentiable genetic and neural risk factors in the two subtypes.

We will trace causal models of AB/CU+ and AB/CU– starting with the behaviour and ending up with genes. Some brief examples of how AB/CU+ and AB/CU– children differ at the behavioural level are provided, followed by descriptions of the cognitive profile associated with AB/CU+ and AB/CU– subtypes. In the subsequent two sections the brain-imaging and behavioural genetic work related to AB/CU+ and AB/CU– is reviewed. The causal modelling approach advocated by Uta Frith and her

colleagues has been of extreme importance in advancing research into development of antisocial behaviour. Current behavioural genetic and brain-imaging research into childhood antisocial behaviour is still awaiting the full “Uta treatment”, but new studies incorporating insights from the causal modelling tradition are on their way. These are discussed in the final section of this paper, and the promise of novel research strategies in advancing timely treatment of antisocial behaviour is emphasized.

(Mis)behaviour

In a longitudinal study conducted a few years ago, CU traits emerged alongside depression and marijuana use as the strongest predictor of later antisocial behaviour (Loeber, Burke & Lahey, 2002). The available evidence indicates that CU traits index a relatively stable characteristic that predicts future antisocial behaviour and particularly poor outcome (Forth, Kosson, & Hare, 2003; Frick & Marsee, 2006; Frick, Stickle, Dandreaux, Farrell, & Kimonis, 2005).

Frick et al. (2005) followed up a group of children from a community sample who were displaying elevated levels of antisocial behaviour with and without CU traits. At each of the four annual follow-up assessments, the AB/CU+ group showed the highest rates of conduct problems, delinquency, and police contact. In fact, this group accounted for at least half of all police contact for the sample in the last three annual assessment points. Furthermore, AB/CU+ delinquency was not limited to aggressive acts, but this group also showed the highest levels of most types of delinquent behaviour (e.g., substance misuse and property offences). In contrast the children who were initially designated to the AB/CU– group were indistinguishable from controls on the trajectory of self-reported delinquency. Although the AB/CU– group did show elevated levels of aggressive conduct problems compared with controls, they were less severe than the AB/CU+ group. AB/CU– children showed a significant increase in police contact only at the last time point of the

study. It was not possible to infer a trend from this one time point, but it may indicate that AB/CU- children begin their involvement in criminal activities later than their AB/CU+ counterparts.

The presence of CU traits has also been shown to be associated with aggression and attitude to punishment. Pardini et al. (2003) demonstrated that a group of delinquent adolescents with high levels of CU traits were more likely to focus on the positive aspects of aggression (i.e., rewards, social dominance) and less likely to be concerned with the negative consequences of committing antisocial acts (i.e., subsequent punishment following the transgression) than were their antisocial peers. These findings held even after controlling for delinquency severity, cognitive ability, and demographic characteristics. In contrast, antisocial behaviour without CU traits is associated with hostile attribution biases (Frick et al., 2003), and children with AB/CU- tend to get distressed about the consequences of their antisocial behaviour (Barry et al., 2000).

Research investigating the effect of parental characteristics contrasting AB/CU+ and AB/CU- groups is scarce. However, two studies have suggested that antisocial behaviour in AB/CU+ children may be less strongly associated with negative and poor parental practices than it is for AB/CU- children (Oxford, Cavell, & Hughes, 2003; Wootton, Frick, Shelton, & Silverthorn, 1997). In addition, Hawes and Dadds (2005) have demonstrated that the use of "time-out" as a method of behaviour modification is less effective in those children with AB/CU+ than in those with AB/CU-.

In summary, CU traits can be used to distinguish two different subtypes of conduct problems at a behavioural level. AB/CU+ is associated with a poorer long-term outcome (Frick et al., 2005), increased severity of antisocial behaviour (Dadds, Fraser, Frost, & Hawes, 2005), and decreased focus on and response to punishment (Hawes & Dadds, 2005; Pardini et al., 2003). AB/CU- is associated with less severe conduct problems, a more favourable response to

discipline, and distress at the consequences of one's own antisocial actions.

Cognitive profile in AB/CU+ and AB/CU-

Just as we can differentiate children with AB/CU+ and AB/CU- at the behavioural level, we can also see some differences in terms of the cognitive-affective difficulties that these children experience. As Uta Frith and her long-standing colleague John Morton have advocated time and again, to understand how behaviour comes about we need to think about cognition (Frith & Happé, 1998; Morton & Frith, 1995). With conduct disorder we are dealing with a behaviourally defined syndrome with different cognitive deficits associated with sometimes similar, but also in part distinct behaviours. In other words, there are several conduct disorders at the level of cognition. In Morton and Frith's causal modelling approach the cognitive level also includes affective processing (henceforth cognitive = cognitive-affective). An important aspect of the causal modelling approach is the maxim that any cognitive account is not merely an alternative way of describing the behaviour in question (Morton & Frith, 1995). In other words, the cognitive elements should not be mapped one for one to the behaviours they are trying to account for. Instead, a model of the underlying cognitive deficit should account for a variety of behavioural phenomena associated with a disorder.

The cognitive deficit associated with psychopathic antisocial behaviour is postulated to be related to a reduction in the salience of punishment information (see Blair, 2006, for a causal model of this subtype of antisocial behaviour). Blair's integrated emotion systems (IES) model works on the assumption that children with AB/CU+ have diminished ability to form stimulus-punishment associations. In childhood, the ability to be able to form associations between moral transgressions and the aversive outcome (e.g., others' distress) is vital for

successful socialization. Individuals with psychopathic traits find the distress cues in others less aversive and therefore are less likely to learn to avoid actions that bring about a negative response. In addition socialization by punishing consequences also relies on ability to form stimulus–punishment associations. Children with AB/CU+ are poor at performing on tasks relying on stimulus–punishment learning. In contrast to AB/CU+, Blair et al. (2006) proposed that in AB/CU– there are elevated levels of anxiety, threat-related reactive aggression and hyperreactivity to threat—for example, angry faces (Dadds et al., 2006; Pardini et al., 2003; Pollak & Sinha, 2002). In line with this suggestion, Viding and Frith (2006) proposed a causal model where at the cognitive level the children with AB/CU– suffer from overreactive emotional intent encoder, which in combination with emotional memory database of maltreatment and hostility will result in a fight response bias. This fight response bias is thought to be triggered in response to acute environmental stressors and results in reactive aggression, impulsive violence, and increased propensity to make hostile attributions to ambiguous situations.

To date, there are only few direct comparisons of the cognitive profile of antisocial children with and without CU traits. Frick et al. (2003) compared groups of nonreferred AB/CU+ and AB/CU– children and found poor processing of punishment information in AB/CU+ and a hostile attribution bias in AB/CU–. Differences have also been observed in emotional reactivity: Loney, Frick, Clements, Ellis, and Kerlin (2003) demonstrated a slower recognition time for negative emotional words in AB/CU+ adolescents, compared with a faster recognition time for the same words in an AB/CU– group. Dadds et al. (2006) reported that CU traits are uniquely related to poor recognition of fearful expressions, while AB/CU– children tended to be hypersensitive to angry expressions. In addition, a large body of research by Blair and colleagues has demonstrated deficits in processing fear, sadness, and punishment in AB/CU+ individuals, as

compared with institutionalized (although not specifically AB/CU–) controls (see Blair et al., 2006, for a review).

“Antisocial” brains

Individual differences in several brain areas and cognitive functions associated with perception and regulation of emotions have been found to correlate with antisocial and violent behaviour (Davidson, Putnam, & Larson, 2000). In particular, the orbitofrontal cortex, cingulate cortex, amygdala, and interconnected regions have shown both structural and functional abnormalities in antisocial populations. Neuropsychological functions associated with these brain regions, such as perception of threat and distress as well as modulation of affective response, are compromised in antisocial individuals (Blair et al., 2006; Moffitt, 2003). Emotionally toxic environments are likely to contribute to these abnormalities in brain function in some, but not necessarily all, antisocial individuals. Unfortunately most of the sparse number of reported brain-imaging studies have not subtyped individuals according to their CU profile and as such are sometimes difficult to interpret. Given the proposed contrasting cognitive profile of AB/CU+ versus AB/CU– it would be informative to study these two subtypes separately.

The IES model proposes that for AB/CU+ individuals, various aspects of amygdala functioning are impaired (e.g., the formation of stimulus–punishment associations). Early amygdala dysfunction may also have a negative impact on the development of empathy (Blair, 2006). The IES model postulates that the cognitive and behaviour profile described above for AB/CU+ individuals is a consequence of amygdala hyporeactivity. In contrast, AB/CU– individuals are proposed to show amygdala hyperreactivity potentiated by early environmental stressors. Blair et al. (2006) suggest that this amygdala hyperreactivity leads to the fight response bias and concomitant reactive aggression but relatively unimpaired social cognition profile observed in AB/CU– individuals.

A handful of functional magnetic resonance imaging (fMRI) studies have studied brain responsiveness to emotional stimuli in callous-unemotional individuals. The most conclusive study to date compared adults with psychopathy (i.e., AB/CU+) with other incarcerated individuals and demonstrated that those with psychopathy show less amygdala activation in when performing an emotional memory task (Kiehl et al., 2001). Another study compared adults with psychopathy and controls matched for age and educational level and reported deficient amygdala activation during fear conditioning (Birbaumer et al., 2005).

Only one fMRI study on children with conduct disorder has investigated brain reactivity to emotional stimuli. Sterzer, Stadler, Krebs, Kleinschmidt, and Poutska (2005) used emotionally significant stimuli and demonstrated amygdala activation in normal children and children with conduct disorder. Compared to the control children, children with conduct problems showed less amygdala activation to threat, as long as anxiety/depression was controlled for in the analyses. No fMRI studies looking at AB/CU+ and AB/CU- children separately have been published to date.

We are currently conducting a large-scale fMRI study investigating neural response to emotional stimuli in typically developing children, as well as children with AB/CU+. Given the scarcity of imaging data for typically developing children and some inconsistency in the results (Herba & Phillips, 2004), a baseline of amygdala response to emotional stimuli needed to be established as a priority. Our study thus sought to first extend the existing literature by replicating the amygdala response to nonsocial emotional pictures and fearful faces in a sample of preadolescent boys in a narrow age range. Although adult data demonstrate that both types of stimuli activate the amygdala, with left laterality for nonsocial emotional stimuli and right laterality for facial emotional stimuli (Hariri, Tessitore, Mattay, Fera, & Weinberger, 2002), to our knowledge, no study to date has provided a direct comparison of amygdala reactivity to nonsocial and social emotional stimuli in children.

Inclusion of AB/CU+ children in our study enables us to compare the strength of the amygdala response to social and nonsocial emotional stimuli in children with AB/CU+ and ability-matched typically developing (TD) children. We are yet to compare AB/CU+ with AB/CU- using fMRI, but this is the natural next step in our research programme. The expectation would be for the children with AB/CU- to show greater amygdala activation than their counterparts with AB/CU+. In summary, studies looking at the specific neural profile of AB/CU+ and AB/CU- are scarce, but there is considerable research interest in this area. As we discuss later in this chapter, it will be particularly important to study how genetic vulnerabilities may manifest at the level of the brain.

In their genes?

The first step in establishing whether genetic influences are important for individual differences in any given behaviour is to conduct twin and adoption studies. As twin studies are the more common of the two, the logic of these studies is discussed briefly here, before some new data regarding heritability estimates for AB by CU subtype are reviewed.

The twin method is a natural experiment that relies on the different levels of genetic relatedness between MZ and DZ twin pairs to estimate the contribution of genetic and environmental factors to individual differences, or extreme scores in a phenotype of interest. Phenotypes include any behaviour or characteristic that is measured separately for each twin, such as twins' scores on an antisocial behaviour checklist. Statistical model fitting techniques and regression analyses methods incorporating a genetic relatedness parameter are used to investigate the aetiology of the phenotype of choice. For further details of techniques in this area see Plomin, DeFries, McClearn, and McGuffin (2000). The basic premise of the twin method is this: If identical twins, who share 100% of their genetic material, appear more similar on a trait than do fraternal twins, who share on average 50% of their genetic material (like any siblings), then we infer that there are

genetic influences on a trait. Identical twins' genetic similarity is twice that of fraternal twins. If nothing apart from genes influences behaviour, then we would expect the identical twins to be twice as similar with respect to the phenotypic measure as are fraternal twins. Shared environmental influences—environmental influences that make twins similar to each other—are inferred if fraternal twins appear more similar than is expected from sharing 50% of their genes. Finally, if identical twins are not 100% similar on a trait, nonshared environmental influences are inferred—in other words, environmental influences that make twins different from each other. The nonshared environmental estimate also includes measurement error.

A wealth of twin studies confirms that individual differences in antisocial behaviour and callous-unemotional traits are heritable (Blonigen, Hicks, Krueger, Patrick, & Iacono, 2005; Larsson, Andershed, & Lichtenstein, 2006; Rhee & Waldman, 2002; Taylor, Loney, Bobadilla, Iacono, & McGue, 2003). Shared environmental influences play some role for individual differences in AB, but not CU. To our knowledge, only two twin studies to date have investigated whether the aetiology of antisocial behaviour differs as a function of CU traits. Although previous research had strongly suggested that children with early onset antisocial behaviour coupled with callous-unemotional traits form a distinct subtype (Blair et al., 2006; Frick & Marsee, 2006), possible aetiological differences between these children and others with early-onset antisocial behaviour had not been studied until recently.

To address this question we first studied teacher ratings of callous-unemotional traits and antisocial behaviour in approximately 7,500 seven-year-old twins from the Twins Early Development Study (TEDS; Viding, Blair, Moffitt, & Plomin, 2005). We separated children with elevated levels of antisocial behaviour (in the top 10% for the TEDS sample) into AB/CU+ and AB/CU− groups based on their CU score (in the top 10% or not). Antisocial behaviour in children with AB/CU+ was under

strong genetic influence (heritability of .81) and no influence of shared environment. In contrast, antisocial behaviour in children without elevated levels of callous-unemotional traits showed moderate genetic influence (heritability of .30) and substantial environmental influence (shared environmental influence = .34, nonshared environmental influence = .26). We have recently replicated the finding of different heritability magnitude for the AB/CU+ and AB/CU− groups using the 9-year teacher data (Viding, Jones, Frick, Moffitt, & Plomin, in press). This difference in heritability magnitude holds even after hyperactivity scores of the children are controlled for, suggesting that the result is not driven by any differences in hyperactivity between the two groups. In summary, our research with preadolescent twins suggests that while the CU subtype is genetically vulnerable to antisocial behaviour, the non-CU subtype manifests a more strongly environmental aetiology to their antisocial behaviour (Viding et al., 2005; Viding et al., in press).

Common behavioural disorders are currently proposed to be the quantitative extreme of the same genetic effects that operate throughout the distribution (Plomin, Owen, & McGuffin, 1994). In this quantitative trait loci (QTL) model many genes are hypothesized to be involved in the development of any behaviour pattern, and these genes are thought to act in a probabilistic manner. There has been slow progress in identifying QTLs, as they are neither sufficient nor necessary to cause extreme behavioural outcome. They can be said to act together with other risk or protective genes to increase or reduce the risk of disorder. Furthermore, risk genes may have to be combined with environmental risk before a clinically significant outcome is produced (Moffitt, Caspi, & Rutter, 2005).

Genes regulating serotonergic neurotransmission, in particular monoamine oxidase A (MAOA), have been highlighted in the search for a genetic predisposition to antisocial behaviour (Lesch, 2003). The MAOA gene is a well-characterized functional polymorphism consisting of a variable number of tandem repeats in the promoter region, with high-activity (MAOA-H) and

low-activity variants (MAOA-L). The MAOA-H variant is associated with lower concentration of intracellular serotonin, whereas the MAOA-L variant is associated with higher concentration of intracellular serotonin. Recent research suggests that genetic vulnerability to antisocial behaviour conferred by the MAOA-L may only become evident in the presence of an environmental trigger, such as maltreatment (Caspi et al., 2002; Kim-Cohen et al., 2006). This research highlights the possibility that increased serotonin availability (often associated with anxiety) in the MAOA-L carriers may serve to increase an individual's vulnerability to environmental risk. The MAOA-L findings appear to be more relevant for the AB/CU- subtype. No molecular genetic studies on CU type of antisocial behaviour exist to date.

Despite the demonstration of genetic influences on individual differences in antisocial behaviour, it is important to note that no genes *for* antisocial behaviour exist. Instead genes code for neurocognitive vulnerability that may in turn increase risk for antisocial behaviour. Thus, although genetic risk alone may be of little consequence for behaviour in favourable conditions, the genetic vulnerability may still manifest at the level of brain/cognition. Imaging genetics studies attest to genotype differences being evident in the brain structure and function in nonclinical samples (Meyer-Lindenberg & Weinberger, 2006). We can think of this as the neural fingerprint, ready to translate into disordered behaviour in the presence of unfortunate triggers. Meyer-Lindenberg and colleagues recently provided the first demonstration of the MAOA-L genotype being associated with a pattern of neural hypersensitivity to emotional stimuli (Meyer-Lindenberg et al., 2006). Specifically they reported increased amygdala activity coupled with lesser activity in the frontal regulatory regions in MAOA-L than in MAOA-H carriers. A recent paper provides further support for the view that a link between the MAOA-L allele and aggression is partly mediated by this pattern of neural hypersensitivity to emotional stimuli (Eisenberger, Way, Taylor, Welch, & Lieberman, in press).

New directions: Imaging genetics of AB/CU+ and AB/CU-

Meyer-Lindenberg et al. (2006) speculate that their brain-imaging findings of poor emotion regulation in MAOA-L carriers relate to threat reactive and impulsive, rather than CU-type antisocial, behaviour. This conclusion is based on the observed amygdala hypo- rather than hyperreactivity in AB/CU+ individuals (Birbaumer et al., 2005; Kiehl et al., 2001). It is thus important to address the potential moderating role of CU on the brain reactivity associated with antisocial behaviour.

A small number of studies have reported increased vulnerability to antisocial behaviour in the presence of the MAOA-H allele (e.g., Manuck, Flory, Ferrell, Mann, & Muldoon, 2000). These may reflect false positive findings, but it is also possible to speculate that the amygdala hypo- as opposed to hyperreactivity seen in CU individuals could be influenced by MAOA-H rather than MAOA-L genotype. This suggestion remains highly speculative, and as for any behaviour, the genetic influences will not be limited to a single candidate gene.

As imaging genetic work on antisocial behaviour is currently in its infancy it has a great opportunity to incorporate lessons learned from the causal modelling tradition (Blair, 2006; Morton & Frith, 1995). We argue that it will be important to employ imaging and cognitive genomics strategies to study how genes to cognition pathways look for different subtypes of antisocial children. Currently such work is undertaken by our own group (using both twin design to measure heritability and measured genotype to estimate the contribution of individual gene effects) and others.

Practical implications

The research reviewed above suggests that there may be a particularly genetically vulnerable group of youngsters for whom early intervention is likely to be crucial to prevent life course persistent antisocial outcome. We would also like to highlight that prevention and treatment

strategies should take into account the different aetiologies of subgroups of antisocial and violent children. Aetiologically heterogeneous samples may explain why intervention programmes can sometimes have mixed results on their success (Frick, 2001; Hawes & Dadds, 2005). Some children seem to respond to well-timed, early prevention and treatment while others do not. We would suggest that the root of this may lie in aetiological differences, particularly differences in cognitive profile of different conduct problem subtypes. The modest to moderate success of intervention programmes may reflect a high success rate with a particular subtype. Frick (2001) has emphasized that while there are prevention programmes available that address the needs of primarily impulsive antisocial behaviour, less is known about possible prevention and treatment of antisocial behaviour in the callous-unemotional subtype.

Research on environmental risk factors within behavioural genetic designs has highlighted a number of important issues. It is more than likely that for children with a vulnerable genotype, this genotype will react with risk environments. Furthermore, at least one of the parents will share the risk genes for antisocial behaviour and is thus more likely to either directly or indirectly contribute to a less than optimal rearing environment. As the parent or parents with the antisocial genotype are not often willing or capable of engaging in efforts for prevention and treatment, these families present a particular challenge for professionals engaged in preventing future, on-going cycle of violence. However, recent successes with nurse visit programmes in breaking the association between maltreatment and antisocial behaviour suggest that genetic risk can be effectively moderated by environmental intervention (Eckenrode et al., 2001; Olds et al., 1997). Some children may only require "milder" environmental risk factors to go down the antisocial path, perhaps due to genetic vulnerability. It is particularly challenging to map out the cognitive profile of these children and make predictions about treatment approaches that capitalize on what is known about cognitive strengths and weaknesses.

For example, children with psychopathic tendencies are strong on self-interest and get motivated by rewards, but do not characteristically process others' distress or react to punishment. These are cognitive strengths and limitations that have to be worked with to produce change in behaviour.

As a final note, behavioural genetic research should caution against entertaining ideas of gene therapy for antisocial behaviour. Genes that have variants that are common in the population are more than likely to have multiple functions, some of which are desirable, others not. Hence, a risk gene may have many functions over and above increasing risk for disorder. When this information is combined with the fact that genes interact in complex systems, as well as with environmental risk factors, it seems pertinent to conclude that removing the effects of one gene via gene therapy is unlikely to be effective (Nuffield Council on Bioethics, 2002).

This does not mean that genotype information will be irrelevant for therapeutic intervention. For example, demonstration of genetically (and consequently cognitively) heterogeneous subtypes of early-onset antisocial behaviour suggests the possibility of subtype-specific risk gene variants that index a risk for different cognitive deficits. An early knowledge of such risk genes may come to guide prevention efforts prior to the emergence of clear, overt behavioural markers for the disorder. As cognitive-behavioural approaches are likely to feature strongly in the antisocial behaviour intervention, developing better understanding of the genes-brain-cognition-behaviour pathways for particular subtypes—especially within longitudinal, developmental framework—could provide crucial insights for intervention.

Summary

One might argue that since we have behavioural tools for reliably indexing who exhibits AB/CU+ and who has an AB/CU- profile, then what do we need causal models and cognitive accounts for? One extremely useful outcome of a

well-articulated model is that it enables specific, testable predictions that go beyond available data and guides further research. This notion is particularly pertinent when thinking about combining different levels of analyses to study development of antisocial behaviour. It will also be important for thinking about treatment approaches. Uta Frith's work on developmental disorders has been extremely important in guiding the current multidisciplinary work on different subtypes of antisocial behaviour. The data from genetic, brain, and cognitive studies to date suggest that AB/CU+ individuals are genetically more vulnerable to antisocial behaviour than are their AB/CU- peers. Adults with AB/CU+ show amygdala hyporeactivity to emotional stimuli, while there is some suggestion that AB/CU- may show the opposite pattern. When compared with each other, AB/CU+ children demonstrate hyposensitivity to others' distress, while AB/CU- children are hypersensitive to anger. New research combining different levels of analyses will no doubt provide further insight about the AB/CU+ versus AB/CU- distinction.

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