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Introduction

The field of violence has rather suffered from a divide between basic laboratory neuroscience and clinical science using non-experimental research strategies. The papers in this special issue sought to bridge this divide and, in so doing, highlight some of the key scientific challenges, as well as the dilemmas and difficulties in the translation of scientific findings (whether basic or clinical) into policy and practice applications.

The time is ripe for such a bridging endeavour owing to the leverage provided by the new technologies of molecular genetics and both structural and functional brain imaging. Also, multiple high-quality long-term prospective longitudinal studies are available (which emphasize the developmental trends and the individual differences that require explanation). Equally, there has been the major expansion of systematic quantitative studies of intervention efficacy. The challenge is provided by the recognition that, up to now, there has been remarkably little crosstalk among these different research approaches. Thus, for example, most of the neuroscience has concerned adults and has mainly involved samples showing extreme behaviours. By contrast, the longitudinal evidence indicates the major age trends that have been found and the importance of dimensions of both risk and psychopathology. Equally, the efficacy studies have been very informative on what does, and does not, 'work' with respect to the broad field of antisocial behaviour, but has largely ignored the role of individual differences that result in different forms of intervention being needed for offenders with different characteristics. The symposium that gave rise to this group of papers in this special issue indicated what can be achieved in integrating neuroscience with clinical practice and policy. In the years ahead, it may be expected that there will be a new generation of research that brings biological measures into the mainstream of longitudinal research, tackles the biological meaning of age trends and uses both of these to examine the mediating mechanisms underlying individual differences in responses to interventions.

The paper by Loeber & Pardini (2008) very usefully summarizes the range of causal questions that need to be addressed. For the most part, neurobiological research has tended to focus on individual differences in the liability to engage in violent behaviour. The implication is that these individual differences are stable over the course of development, but longitudinal studies have been clear-cut in showing that substantial changes take place over time (see Sampson & Laub 1993; Laub & Sampson 2003). The second type of causal question, therefore, concerns the origins of general developmental trends—the rise in physical aggression in the early pre-school years (Côté *et al.* 2006), followed by the fall during middle and later childhood (Nagin & Tremblay 1999), but then a peak in offending that includes serious violence in late adolescence (Rutter *et al.* 1998). As Loeber & Pardini note, on the whole there is a tendency for a progression from minor aggression, through physical fighting, to very serious violence.

The third type of causal question also focuses on developmental trends but differs in focusing on individual differences in course as they relate to variations in life circumstances—as reflected, for example, in marriage (Sampson *et al.* 2006), or being a member of a delinquent gang (Thornberry *et al.* 1993). The findings (not considered in the papers in this special issue) clearly point to the environmental influence of psychosocial features. What they do not do, however, is to determine whether neurobiological features affect individual susceptibility to such environmental forces.

A fourth, yet again different, causal question concerns group differences, such as the major sex difference in antisocial behaviour (see Moffitt *et al.* 2001) or the ethnic variations (see Rutter & Tienda 2005). Do their origins reflect the same neurobiological or psychosocial influences that operate within these broad groups? Up to now, there has been very little serious attempt to tackle that question. Somewhat comparable issues arise with respect to the very major secular changes in the overall rate of crime in the last half century or so (Rutter & Smith 1995).

Finally, there are the situational influences on whether any particular individual engages in violence on this occasion (and not some other) or in that social circumstance (see Rutter *et al.* 1998). There has been a tendency to focus on psychosocial situational factors but the parallel neurobiological question concerns the possible role of alcohol or other drugs in predisposing to violence through the removal of inhibitions (see Tonry & Wilson 1990; Ito *et al.* 1996; White *et al.* 2002). It is important to appreciate that mediation may lie either in the chemical effect of the substance or from the impulsive, reckless lifestyle of substance users.

It is often assumed that violent crime differs in its origins and meaning from non-violent acquisitive crime, such as theft (see Rutter *et al.* (1998) for a succinct discussion of the evidence). A key methodological problem is that most offenders commit a wide range of offences; specialization is the exception rather than the rule. It has been found that the greater the number of offences, the greater the likelihood that at least one will involve violence. Owing to the substantial overlap between recidivist crime and violence, any study of violence needs to take that into account, and few have done so. As discussed in other papers in this

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journal, it is also crucial to appreciate that violent crime itself is heterogeneous, with the distinctions among instrumental aggression (i.e. to further some purpose such as theft), angry aggression (i.e. a response to a provoking situation) and 'sadistic' aggression (i.e. violence that seems to be intrinsically rewarding) possibly particularly important.

Odgers, in her paper,[1] uses developmental trajectories to tackle a particular pathway distinction, namely Moffitt's (1993) postulate of the distinctions between *lifecourse-persistent* (LCP) and *adolescent-limited* behaviour. Numerous studies have shown that LCP begins in childhood and there has been the general assumption that the key driving force lies in an unusually early age of onset. Her trajectory analyses are critically important in showing that childhood-limited (CL) antisocial behaviour is very common, with only a third going on to follow an LCP path (Odgers *et al.* 2007*a*). The key question is what drives the persistence into adult life. The findings showed that a range of childhood variables (including attention deficit hyperactivity disorder) are associated with LCP and are much less frequent in CL, but a family history of antisocial behaviour or alcohol problems was also an important differentiator (Odgers *et al.* 2007*b*). Although, in her published papers, Odgers interpreted the findings differently, the evidence suggests that the early onset is more likely to be a proxy indicator of some important liability, rather than a cause in its own right. At the very least, research needs to be undertaken to test that possibility. Her paper also discussed the important association between antisocial behaviour and physical ill health, in order to emphasize the need to test alternative mediating mechanisms for the association.

Hodgins (2008) raises the important question of possible heterogeneity in antisocial behaviour generally and in violence in particular. The issue derives from the well-documented associations between schizophrenia and aggressive behaviour. Most individuals with schizophrenia do not engage in serious violence but the proportion of those who do is greatly raised over the general population base rate. She discusses the possibility that part of the association derives from drug misuse, but mainly puts forward a tripartite typology. The first group consists of individuals with early-onset antisocial behaviour that precedes the onset of psychosis but yet persists. In this group, the antisocial behaviour is part of the pattern of precursors for schizophrenia and the causal influences probably do not differ greatly from those for antisocial behaviour in the absence of psychosis. The second group is different in that they did *not* show antisocial behaviour in childhood and the third group is similar in that respect but differs in their callousness and lack of remorse. She queries whether the deficits associated with schizophrenia make it more difficult for the individuals to learn not to be aggressive.

Viding *et al.* (2008) use twin study findings to ask a similar question about possible subtypes of antisocial behaviour. Their focus, however, is not on schizophrenia but rather on psychopathy as manifest in the form of callous–unemotional traits. Their findings show a higher heritability for antisocial behaviour associated with psychopathy than for antisocial behaviour that is not accompanied by these traits. They argue that because psychopathy involves a lack of response to others' distress, it may require different forms of intervention. Their paper is also important in noting that genetic influences may operate through either gene–environment correlations or interaction (G×E), as well as through main effects. Caspi's paper (see below) returns to this theme.

Hill *et al.* (2008) deal with emotional responses in a very different way in their longitudinal study, from 18 months to 5 years of age, of the children of mothers with post-natal depression, together with a control group. Security of attachment was used at 5 years to assess intentionality (meaning an interpretation in terms of emotions), and conduct disorder symptoms were assessed by teachers' questionnaire at the same age. The findings showed that responding in the intentional stance in the high threat scenario had a significant effect in the postnatal depression group but not in the controls. Similarly, insecure attachment had effects only in the high threat condition. A mediation analysis showed that the lack of use of intentionality provided the route to conduct problems. The attempt to assess mediation was informative and the findings are compatible with a rather different emotional response to that associated with psychopathy. Caution is required owing to the small sample size, the cross-sectional nature of the findings at 5 years and the lack of any demonstrated connection with violence.

Caspi's paper[1] developed the theme of G×E introduced by Viding *et al.* His research was different in being able to use molecular genetic identification of individual susceptibility genes in conjunction with measurement of environmental risks. The findings (since replicated and confirmed by a meta-analysis; see Taylor & Kim-Cohen 2007) showed that a functional polymorphism in the gene encoding the neurotransmitter-metabolizing enzyme monoamine oxidase A (MAOA) moderated the effect of maltreatment (Caspi *et al.* 2002). Maltreated children with a genotype conferring high levels of MAOA expression were much less likely to develop antisocial problems or commit a violent offence. There are important methodological hazards to be overcome in studying G×E (see Rutter 2008) but the findings are potentially very important in pointing to possible biological pathways that bring together the effects of G and E (see Caspi & Moffitt 2006; Rutter 2007). Uncertainties remain on whether the G×E concerns responsivity to the environment or susceptibility to adverse environments (from an evolutionary perspective, the former seems more probable). Similarly, it has yet to be established whether the G×E particularly concerns violence as such, rather than recidivist crime that just includes violence as one of many forms of antisocial behaviour. A further challenge is presented by the need for more direct studies of the neural effects. Meyer-Lindenberg *et al.* (2006) have shown how this can be achieved through structural and functional brain imaging.

Patrick (2008) provides an important additional perspective on the same theme through his integrative review of psychophysiological studies. He differentiated between *causal* studies (such as those by Caspi),

biomarker studies focusing on biological differences that distinguish between aggressive and non-aggressive individuals, and *process* studies that seek to identify how aggressive individuals may be distinctive in their biological (including psychological) processes of stimuli and events. Both functional magnetic resonance imaging and electrocortical response measures (such as those provided by EEG and event-related potential responses) constitute important research strategies. He noted the substantial evidence that aggressive individuals tend to show a lower than usual level of autonomic arousal combined with higher autonomic reactivity, but also the substantial evidence that markedly different results are found with individuals showing psychopathy. Up to now, process studies have tended to study psychopathy as a syndrome and, hence, have not examined separately the two components of emotional callousness and antisocial deviance (including aggression). Similarly, most research into aggression in individuals without aggression has not adequately differentiated between vulnerability to a broad range of antisocial behaviour, drug/alcohol problems and disinhibiting behaviour and aggression *per se*. Patrick considers two alternative integrative conceptual models: one focusing on the variety of impulse control problems and the other based on a neurobiological model reflecting dysfunction in a set of interconnected brain systems. Clearly, the challenge is to bring these two approaches together.

Blair (2008) attempts to do just this in his discussion of findings on psychopathy. He argues that any neurobiological model would have to account for both the emotional dysfunction and the increased risk for reactive and instrumental aggression associated with psychopathy. He reports that the amygdala is crucial for responding to fearful emotional expressions that serve to reinforce stimulus-reinforcement learning, which is crucial for socialization. The ventromedial prefrontal cortex is also critical for the representation of reinforcement information because impairment is likely to lead to impaired decision making. There is substantial research (mainly with adults) that has given rise to findings that are compatible with this model and, without doubt, it constitutes a most valuable way of approaching the challenges. For the reasons already noted, however, key questions remain to be investigated.

Dadds & Rhodes (2008) directly take up the challenge of seeking a synergy between specific biological processes and psychological experiences as they unfold developmentally. They start by noting the extensive evidence that behavioural interventions focusing on parenting have a substantial effect in reducing violence and antisocial behaviour, but go on to focus on the neglected question of heterogeneity in response associated with child characteristics. Their own work found that young boys with callous–unemotional traits were less responsive to these parenting interventions. They argued that the reduced recognition of, and response to, fearful expression might be a function (at least in part) of failing to look at the eyes of stimulus faces. Strikingly, their findings supported this hypothesis. They went on to note the emerging data showing that manipulations of the serotonin system may directly influence facial emotion processing. Both human and animal studies seem to suggest that serotonergic dysfunction (which is associated with adverse experiences) is particularly related to thresholds for explosive violence, whereas low cortisol is associated with 'cold', more predatory, violence.

Dadds & Rhodes conclude by seeking to bring these findings together in order to raise possibilities for innovative interventions. They argue that what is needed now is the use of neuroscience findings to consider both how specific parenting strategies might be adapted to deal with individual differences in emotional sensitivity, and how drugs might be employed to enhance psychological effectiveness. With respect to the latter, they instance the neuropeptide oxytocin that enhances social recognition and approach behaviour, and D-cycloserine that strengthens extinction of learned fear memories, thereby possibly enhancing their later retrieval. With respect to the former, they point to the possible value of helping emotionally callous children to focus on the salient aspects of emotional situations. The authors are explicit that these are futuristic approaches that have yet to be tried and tested but what they propose would serve to capitalize on the possibilities of integrating neuroscience and clinical science as applied to the remediation of violence.

McGuire (2008) echoes Loeber & Pardini's emphasis on both the range of causal questions that need addressing and the heterogeneity of aggressive behaviour (including the massive number of killings associated with war and with genocide). In the biological investigation of individual differences, it is crucial not to lose sight of the fact that many people will resort to violence when there is intergroup conflict. Moreover, the deaths associated with war and genocide far outweigh those due to personal violence. The risk factor for individual differences in propensity to engage in violence may, or may not, be the same in the two cases, but we must not neglect the powerful social forces predisposing to (and often used to justify) group violence.

Against that background, McGuire presents an authoritative overview of the evidence on the efficacy of interventions designed to reduce aggression and violence. He concludes that there is reasonably good evidence that emotional self-management, interpersonal skills training, problem-solving strategies and allied training approaches show mainly positive effects of a worthwhile kind. On the other hand, attention is drawn to the lack of focus on subgroup differences in responsiveness, such as those claimed to be associated with psychopathy. At least as seriously, relatively little is known on the factors mediating beneficial effects (or those mediating treatment resistance). By the same token, despite the general acceptance of multiple pathways to the same endpoint, very little research has investigated the different types of interplay among causal factors, including moderator and mediation effects (see Baron & Kenny 1986; Kraemer *et al*. 2001).

Duggan (2008) provides a dose of reality testing by insisting that a considerable gap remains between scientific evidence and clinical practice, at least as viewed in relation to the pattern of antisocial personality disorder (ASPD). He argues that one of the

problems lies in the breadth of the impairments associated with ASPD and the lack of consensus on how it should be conceptualized. Another problem concerns the leap required in moving from neuroscience to clinical need. Duggan suggests that a unifying theory is needed to bring together the clinical findings in order to identify mechanisms that address treatment responsiveness variations. It is suggested that that should now be possible. Whether or not the clinical concept of personality disorder constitutes the best way forward in understanding violence is uncertain. Maybe the future should lie in examining the connections between brain functioning and individual differences in violent behaviour.

The final article by Tremblay (2008) focuses on prevention of the onset of physical aggression rather than its remediation once it has become established. Very reasonably, he argues that we need to differentiate between actual physical aggression and general disruptiveness, misbehaviour and antisocial behaviour. When that distinction is made, the empirical evidence points to an onset of physical aggression in the pre-school years. Tremblay suggests that the greatest interest, therefore, should be in the trajectories over time and the differences between those who learn not to aggress and those who continue to do so. Although that is indeed a pertinent issue, we should note that relatively stable differences remain over time among individuals. The largest difference lies between those who never exhibit aggression to any significant degree and those who persist in doing so throughout the whole of the developmental period. Tremblay argues that more attention needs to be paid to G×E and to the possibility of epigenetic effects by which experiences alter gene expression. Some researchers may query the assumption that most experiential effects operate through epigenetic mechanisms (clearly alternative possibilities need to be examined and tested), and other researchers will point to the limitation that gene expression tends to be tissue specific. Lymphocyte studies may provide clues on methylation patterns, but extrapolation to the brain is tricky. That is, of course, where animal models could be informative. To what extent do methylation patterns in lymphocytes reflect patterns in the brain? More particularly, what would be lost by the inability to link methylation patterns to particular genes operating in particular parts of the brain? Nevertheless, there should be a general welcoming of Tremblay's plea for more use of experimental designs that can use intervention findings to test causal hypotheses.

The symposium provided much fruitful discussion on the challenges and solutions involved in integrating basic and applied neuroscience and the papers in this issue should do the same. The focus throughout was on violence and the problems associated with it. However, the background was provided by the general awareness of the need to consider what is meant by a 'cause' when dealing with multifactorial traits or disorders, and of the ever present need to combine research strategies when seeking to identify component causes (Academy of Medical Sciences 2007). There is good neuroscience that is potentially relevant to clinical practice and there are good clinical studies that highlight the heterogeneities that must be considered. It is not just a question of going from the bench to the bedside. Rather, what is required is a creative two-way iterative interplay among basic neurosciences, clinical science and applications in the field. These papers provide a host of useful leads as to how this might proceed.

ENDNOTE

[1]An invited paper at the meeting but which is not included here for practical reasons.

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