

Continuities and discontinuities in psychopathology between childhood and adult life

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The possible mechanisms involved in continuities and discontinuities in psychopathology between childhood and adult life are considered in relation to the findings from systematic, prospective, long-term longitudinal studies. Findings on schizophrenia, neurodevelopmental disorders, emotional disturbances, antisocial behaviour and substance abuse are used as conditions illustrating the key issues. The overarching themes are then discussed in relation to heterotypic continuity and psychopathologic progression, early age at onset and a range of possible mediating mechanisms – including genetic mediation, ‘kindling’ effects, environmental influences, coping mechanisms and cognitive processing of experiences. Some of the key research challenges that remain concern the testing of competing hypotheses on mediating processes, the changes involved in adolescence, the transition from prodromal phase to overt schizophrenia and the emergence of adolescent-limited antisocial behaviour. Greater use needs to be made of genetic research strategies and of the testing of possible cognitive processing mediation effects. **Keywords:** Heterotypic continuity, precursors/prodromata, age at onset, genetics, adolescence.

When the associations between mental disorders in childhood and adulthood were reviewed a decade ago (Rutter, 1995), the main conclusion was that the findings raised key questions about possible causal mechanisms – the circumstances in the biology or in the environment that make continuities or discontinuities either more or less likely. Similar conclusions were drawn in reviews of the concept of developmental psychopathology (Cicchetti & Cohen, 1995; Rutter & Sroufe, 2000) and of a developmental perspective (Rutter, 2005).

The possibility of examining mediating processes has come about partly as a result of the availability of a range of high quality long-term longitudinal/epidemiological studies (most with repeated, multi-method assessments) extending from childhood into adult life, partly because of new thinking on concepts and new findings on mechanisms, and partly because of a virtual revolution in research and theoretical approaches to the topic of continuities and discontinuities between childhood and adult life (Maughan & Kim-Cohen, 2005). A generation ago, very few psychiatrists and psychologists dealing with adult mental disorders would have considered a developmental perspective as appropriate, let alone necessary. That is no longer the case today. A developmental perspective is mainstream.

This review primarily focuses on the possible mechanisms underlying continuities and discontinuities over the life span, rather than seeking to quantify the overall level of association between psychopathology in childhood and in adult life.

Instead of dealing with the whole range of psychopathology we have chosen to review the evidence on a few disorders that most readily illustrate the issues that we wish to highlight. These comprise schizophrenia, neurodevelopmental disorders, emotional disturbances, antisocial behaviour and substance abuse. In reviewing these areas, we have relied on prospective, longitudinal studies that began before the age of 16 and which continued until the age of 21 years or later, but we have made occasional reference to the findings from retrospective data when they were critical for the questions being examined. After considering the evidence on specific disorders, we draw together some overarching themes.

Childhood origins of schizophrenia

Traditionally, schizophrenia was conceptualised as a psychosis, usually beginning in late adolescence/early adult life. Nevertheless, early case-control and follow-back studies (Rutter & Garmezy, 1983) showed that children who later developed overt schizophrenia were more likely than controls to show social, emotional and behavioural problems in childhood. Moreover, the longitudinal study of children born to mothers with schizophrenia (as compared with children born to mothers with an affective disorder, and with controls) has shown that those who develop a schizophrenia spectrum disorder exhibit a stable pattern of impaired attention (Cornblatt, Obuchowski, Roberts, Pollack, & Erlenmeyer-Kimling,

1999). This does not alter with the onset of illness or with environmental circumstances, unlike the behavioural difficulties that fluctuate over time. Total population epidemiological/longitudinal studies provided a stronger test of the suggestion that abnormalities in childhood constituted precursors of schizophrenia that did not become manifest until early adult life. The precursors include delays in early motor development and impairments in receptive language and cognitive functioning. The associations with schizophrenia are independent of the effects of socio-economic, obstetric and maternal factors (Cannon et al., 2002; Isohanni, Murray, Jokelainen, Croudave, & Jones, 2004). The Finnish longitudinal study showed that the impairments were evident as early as one year of life and showed greater continuity over time in those who later developed schizophrenia than among normal controls or those with other forms of psychiatric disorder (Isohanni et al., 2004). The Dunedin longitudinal study also provided strong evidence that the associations were present only among children later diagnosed as having a schizophreniform disorder. In view of the possibility of genetic overlap between schizophrenia and bipolar disorder, it is important that the neurodevelopmental abnormalities are not found in children who later develop bipolar disorder (Murray et al., 2004). What is not entirely clear, however, is whether these neurodevelopmental impairments reflect early manifestations of a genetic liability or, rather, the effects of some independent environmental risk factor. There is evidence of significant associations between various prenatal risk factors and the later development of schizophrenia, but probably not mediated by the neurodevelopmental precursors in childhood (Cannon, Kendell, Susser, & Jones, 2003; reviewed by Lewis & Levitt, 2002; Marengo & Weinberger, 2000; Rapoport, Addington, & Frangou, 2005).

Like the earlier studies of special groups, the general population prospective studies have confirmed that overt schizophrenia in adulthood is frequently preceded by socio-emotional behavioural disturbance. Unlike the neurodevelopmental impairment findings, however, the associations apply to a range of other adult psychiatric disorders and are, therefore, of little use in identifying specific precursors of schizophrenia. Home movies (Schiffman et al., 2004; Walker, Grimes, Davis, & Smith, 1993) tell much the same story. That is to say, children who later show overt schizophrenia differ from other children in both socio-emotional features and motor coordination. Findings on child psychiatric clinic attendees who go on to develop either schizophrenia or bipolar disorder, nevertheless, suggest that there may be a degree of diagnostic specificity (Cannon et al., 2001), with abnormal suspiciousness/sensitivity and relationship difficulties with peers being particularly associated with later schizophrenia.

The earlier studies of special groups had given no strong indication that these childhood precursors included any early manifestations of psychotic symptomatology. The findings from the Dunedin Longitudinal Study, however, were important in providing the first evidence for continuity of psychotic-like symptoms from childhood to adulthood. Self-reported symptoms about delusional beliefs and hallucinatory experiences at age 11 were significantly associated with an increase in the risk of developing a schizophrenia spectrum disorder by the age of 26 years (Cannon et al., 2002; Poulton et al., 2000).

Important new data have also been provided by findings from the Edinburgh high-risk study (Johnstone, Ebmeier, Miller, Owens, & Lawrie, 2005). A high-risk sample of 163 young people aged 16 to 24 years with two relatives having schizophrenia were compared with 36 controls in relation to whether or not they developed schizophrenia over the subsequent eight years. Findings showed that of those at high risk, 20 developed schizophrenia within a period of $2\frac{1}{2}$ years, and rather more experienced isolated or partial psychotic symptoms. The results so far have shown that schizotypal symptoms and cognitions provided the best differentiation between the familial high-risk subjects who did and who did not develop psychotic symptoms. Neuropsychological and neurodevelopmental measures, in keeping with other research findings, differentiated individuals at high risk from healthy controls but they were not very effective in differentiating within a high-risk group those who would go on to develop schizophrenia.

Three main queries have yet to be resolved with respect to the meaning of the findings on the features in childhood and adolescence that predict the later development of a schizophrenic psychosis. First, distinctions have usually been drawn between precursors and prodromal symptoms, the difference being that the former constitute risk factors, whereas the latter constitute the early manifestations of the disorder itself. The general notion is probably valid but over half of individuals with prodromal features do not go on to develop schizophrenia (Drake & Lewis, 2005). Accordingly, this necessarily raises queries about what is meant by a prodromal phase (Cannon et al., 2003). The uncertainties over the meaning of prodromal features necessarily mean that there should be similar uncertainties over the appropriateness of intervening clinically during this phase (Corcoran & Malaspina, 2005), but it may be justified if there is impaired functioning, perhaps especially if there is a familial high risk. To an even greater extent, the uncertainties over intervention apply to the psychotic-like symptoms identified at an even earlier stage.

Second, all the findings raise the question of what it is that leads to the translation of precursors or

prodromata into overt schizophrenia. Three main possibilities have been considered. To begin with, developmental changes in brain structure and function during late adolescence may be crucial (Keshavan, Kennedy, & Murray, 2004). It is quite likely that such brain changes are important but they do not account for the fact that the transition from precursors and prodromata to overt psychosis occurs in only a minority of individuals. Alternatively, as consistently shown by epidemiological/longitudinal studies, heavy early use of cannabis in adolescence is associated with a substantial increase in the risk of schizophrenia (Arseneault, Cannon, Witton, & Murray, 2004; Henquet et al., 2005). This risk does not apply to occasional recreational use and it does not apply to heavy use that begins only in adult life. In addition, the risk seems to apply mainly to those individuals who had shown either precursors or prodromata of schizophrenia spectrum disorders. Caspi et al. (2005) have now shown, using the Dunedin longitudinal study data, that the effect of early heavy cannabis use leading to a schizophrenia spectrum disorder is a function of the valine allelic variation in the catechol-O-methyltransferase (COMT) gene. The finding has yet to be replicated but, if confirmed, it will point to a possible mechanism for the transition into overt schizophrenia. Caspi et al. (2005) have been at pains to point out, however, that this gene-environment interaction could account for only part of the population variance in the transition. Most of the individuals with the specific allelic variation, who use cannabis heavily, do not develop schizophrenia and many individuals who do develop schizophrenia have not shown heavy cannabis use. Nevertheless, the evidence suggests that this is likely to play a role in the transition that occurs in late adolescence and early adult life. The third possibility is that certain types of social adversity, such as migration and isolation, may also be contributory (Broome et al., 2005).

The final query concerns the possibility that, despite the early neurodevelopmental abnormalities, there are further changes in both cognitive function and brain structure and function that take place during the course of the schizophrenia spectrum disorder in adult life either as a result of the disease process or of the drugs used in its treatment (Keshavan et al., 2004). The evidence so far is not decisive but it does suggest that further changes may take place after the development of the psychosis and, therefore, that these may be relevant with respect to continuity in psychopathology.

Neurodevelopmental disorders

In recent years there has been a tendency for certain early-onset disorders to be grouped together under the concept of 'neurodevelopmental disorders'. Such disorders have eight main features. First, they are

manifest by a delay/deviance in maturationally-influenced psychological features (i.e., the skills cannot develop unless the necessary neural structure is available). Secondly, the course of the disorder is not marked by the remissions and relapses that are characteristic of most multifactorial mental disorders. Third, there is a general tendency for the impairment associated with the disorder to lessen with age, but this goes in parallel with a tendency for it to persist into adulthood. In other words, the disorder is not just a normal variation. Fourth, the disorders all involve some degree of specific or general cognitive impairment. Fifth, there is a tendency for overlap among the different neurodevelopmental disorders. That is, although each disorder has some important specificities they also have substantial overlap with other neurodevelopmental disorders. Sixth, in almost all cases, the genetic influences on individual differences and liability are quite strong. Seventh, despite this, environmental influences are probably also contributory. Finally, the disorders all show a marked male preponderance. In this review, we focus on the evidence with respect to continuities in these disorders between childhood and adult life, simply noting key references giving details of other aspects of the disorder. In each case, the findings on persistence into adult life involve a mixture of the expected and unexpected and substantial challenges remain in the identification of the key mediating factors.

Autism spectrum disorders

The heritability of autism exceeds 90% but it is a multifactorial disorder, the environmental risk factors remaining unknown at the present time (Sigman, Spence, & Ting Wang, in press). Home movies have shown that abnormalities may be detectable in the first year of life but most children with autism do not show readily identifiable abnormalities until about 18 months of age, with reliable and valid diagnoses being possible only after the age of 2 years in many cases (Rutter, Le Couteur, & Lord, 2003).

Earlier follow-up studies of individuals with an autism spectrum disorder (reviewed by Howlin, Goode, Hutton, & Rutter, 2004) showed that prognosis for those with an initial non-verbal IQ in childhood of less than 50 was uniformly poor, with none achieving independence in adult life and all showing continuing handicapping autistic problems. Accordingly, the main interest lies in what has happened to those individuals with a performance IQ of 50 or more, who have been followed into adult life.

The most systematic data have been provided by a comparative study of autism and developmental receptive language disorders (Howlin, Mawhood, & Rutter, 2000; Mawhood, Howlin, & Rutter, 2000) and by the long-term follow-up undertaken by Howlin

et al. (2004). The latter followed a sample of 68 individuals who had a mean age of 7 years when first seen and a mean age of 29 years at follow-up. Overall, scarcely any individuals had ceased to show autistic features but many had continued to make progress since they were seen in childhood. A fifth had attained some academic qualifications at school and five had gone on to college or university, with two studying at a post-graduate level. Almost a third were employed and around a quarter were described by parents as having some friendships involving shared interests or activities. In keeping with earlier findings, the best predictor of outcome was the IQ level and the presence of useful language by the age of 5 years.

Nevertheless, there were several surprising findings among the results. Thus, although the best outcomes were entirely confined to the group who had an initial performance IQ of at least 70, even among those showing initial normal scores on non-verbal cognitive tests, only a sixth had a very good outcome – meaning that they were in paid employment, had some friends and had a substantial level of independence. About the same proportion had a good outcome, but nearly half had a poor or very poor outcome – meaning that they were in residential accommodation offering very limited autonomy, or were living at home and were dependent on their family. It remains unclear whether this continuing degree of impairment reflects the severity of the basic biological handicap, or inadequacy of services in childhood, or the inadequacy of services in adult life. The last probably plays some role in that there is some indication that more extensive and appropriate help with independent living and employment in adult life may make a real difference (Mawhood & Howlin, 1999).

The second unexpected feature is that although an IQ in the normal range was predictive of a somewhat better outcome, variations in IQ within the range above 70 were of negligible prognostic importance, and it is not clear why. The other important feature was the peak age of onset of epilepsy in late adolescence or early adult life, which has been shown in other studies (Deykin & MacMahon, 1979; Rutter, 1970) and which is strikingly different from the usual age of onset in either the general population or in mentally retarded samples. It may be assumed that this unusual age of onset is likely to have some neuropathological significance but quite what this is remains unknown. The other uncertainty is that these findings all concern individuals with autism as traditionally diagnosed and much less is known about the adult outcome for those with the milder varieties of autism now usually described in terms of a so-called broader phenotype. The available evidence indicates that a much higher proportion of those do achieve independent functioning in adult life, although what the proportion is remains

uncertain, and it does appear that, despite their good functioning in many respects, they continue to show important autistic features.

Specific language impairment (SLI)

Traditionally, concepts of developmental language disorders (specific language impairment: SLI) have assumed that these represent a relatively pure deficit in language. The Clegg, Hollis, Mawhood, and Rutter (2005) follow-up from childhood into mid-adult life has cast considerable doubt on that concept. The groups studied were confined to males with a non-verbal IQ in childhood of at least 70. In that respect, they represented a sample without additional cognitive impairment but they comprised the more severe disorders with respect to the requirement that receptive language had to be impaired. The individuals were followed up initially into early adolescence and then into early adult life, with the Clegg et al. (2005) follow-up taking the measurement forward to the mid-30s. This latest follow-up involved a systematic comparison with both the non-affected siblings and also an IQ-matched population control group. All of the individuals studied had gained a reasonable level of communicative language, but their scores on tests of language functioning were all far below those of both their siblings and the IQ-matched control group (the latter two groups not differing significantly on any of the outcomes assessed). Not surprisingly, the specific language impairment group was also significantly impaired in adult life on both reading and spelling.

What was much more unexpected, however, was that only just over one in six of the SLI group had been continually in paid employment, as compared with some 94% of their siblings. Moreover, one in six had never had paid employment, this applying to none of either of the two comparison groups. The majority (nearly three-fifths) were not living independently; over half had some impairment in their friendships; and only just over a quarter had ever had a cohabiting relationship, as compared with 100% of their siblings and over 90% of the IQ-matched comparison group. In short, although subtle language deficits continued right into mid-adult life, the main impairment in adulthood concerned social functioning and social relationships, rather than language. It is also surprising that, although the overall outcome tended to be better among those with the least severe language impairment in childhood, the associations were quite weak. Interestingly, too, the SLI group showed significant impairment in theory of mind task performance.

Overall, in keeping with the findings from other studies (Bishop & Norbury, 2002; Botting & Conti-Ramsden, 2003; Stothard, Snowling, Bishop, Chipcase, & Kaplan, 1998), four findings stand out. First, although there are children who are very delayed in their onset of spoken language who nevertheless

catch up and appear to show normal functioning from the time of school entry, at least as high a proportion go on to show language difficulties that persist right into adult life. In that respect, it is clear that the disorder represents far more than the end of a normal continuum. On the other hand, twin data (Bishop, North, & Donlan, 1995) showed that the genetic liability spans both mild and severe language impairment and also includes both highly specific and rather more general language problems. Second, although there are important differences between autism and SLI, there is also substantial overlap, especially in those whose language deficit includes pragmatic problems. Third, genetic influences seem to be substantially greater in the case of persistent language impairment resulting in clinical care, as compared with transient delays in language development (Bishop, Price, Dale, & Plomin, 2003). Fourth, although SLI is defined in terms of a language impairment, the adult outcome indicates that it actually involves a much broader deficit that is social (and social cognitive) as much as linguistic.

Dyslexia

As with autism, the developmental pathways issues in relation to dyslexia involve looking both backwards into infancy, before reading is possible, and forwards into adult life. For obvious reasons, dyslexia can only be diagnosed after a child has reached the age at which it would normally be expected to be able to read. Nevertheless, the prevailing concept of dyslexia is of a genetically influenced neurodevelopmental disorder that has its origins in linguistic and cognitive deficits manifest in the pre-school years. The extent to which this is empirically justified has been tested by the prospective study from infancy of children thought to be at high risk because of a familial loading for reading disabilities. Thus, the Jyväskylä longitudinal study of dyslexia (JLD) followed the development of 107 children at familial risk of dyslexia, comparing them with 93 controls (Lyytinen et al., 2004). Evoked response potential (ERP) experiments were conducted in the neonatal period to examine brain responses to speech sounds. Some significant differences between the two groups were found, although the magnitude of the differences was not sufficient for this to be useful at an individual diagnostic level. The same applied to the ERP experiments undertaken at six months and the discrimination performance at the same age as measured by a conditioning paradigm.

The meaningfulness of these between-group differences was shown by the finding that they were related to later language skills. Perhaps surprisingly, however, the groups did not differ with respect to measures of receptive or expressive language during the age period from 12 to 13 months. There were some significant differences at 3½ years but they

were substantially greater by age 5 years. The associations between early language and reading at age 7 years (when reading instruction begins in Finland) were greater in the at-risk group than in the control group. The findings, considered as a whole, indicate that the cognitive/language deficits associated with dyslexia are indeed present in the early years of life, at least in those with an increased familial risk for dyslexia, but these are not sufficiently distinctive to be used for diagnosis at an individual level.

There have been various follow-ups into adult life of specialised samples of individuals with dyslexia but the only data on representative general population samples derive from the London and Isle of Wight studies (Maughan & Hagell, 1996; Maughan – personal communication). Some four-fifths of the Isle of Wight group of individuals who showed a reading disability in childhood had spelling scores at age 44/45 years that were at least two standard deviations below the general population mean, as compared with only about one in twenty of the comparison group without a reading disability in childhood. A follow-up to the early 20s of a London general population sample (Maughan & Hagell, 1996) showed that four-fifths of individuals who had had a reading disability in childhood had a reading age of less than 12 years at follow-up, compared with less than 1 in 25 of controls. The continuing reading problems had constrained educational achievement and, both directly and indirectly, also occupational options and material circumstances in early adult life. Despite this, those with dyslexia did not show any increase in adult mental disorders. The interviews suggested that good outcomes were fostered by sensible niche-picking and supportive partners.

The Isle of Wight study findings in childhood (Rutter, Tizard, & Whitmore, 1970) had shown the high frequency with which reading difficulties were associated with antisocial behaviour. The same findings have been reported in numerous other studies. It might be thought that the association was so marked that it meant an intrinsic, inbuilt co-occurrence. The follow-up into adult life, however, negates this view in that there was no excess of criminality or aggressive behaviour found among men with childhood histories of reading problems (Maughan, Pickles, Rutter, Hagell, & Yule, 1996).

Over the years, there has been some controversy over the concept of dyslexia as a categorically distinct condition (see Démonet, Taylor, & Chaix, 2004; Rutter & Maughan, 2005). The adult outcome findings clearly indicate that the presence of a substantial reading disability in middle childhood/early adolescence constitutes an impairment that shows a high degree of persistence into adult life. On the other hand, this does not necessarily mean that, at a basic level, dyslexia constitutes a qualitatively distinct category. Indeed, Snowling, Gallagher, and Frith (2003), in their comparison of children who had a first-degree relative with dyslexia and controls,

argued that dyslexia was likely to be dimensional because the children in the familial risk group without dyslexia at age 8 nevertheless scored below controls on tests of grapheme–phoneme knowledge. In keeping with the evidence on both SLI and autism, the findings suggest that dyslexia is not just the end of a normal continuum of reading skill. Nevertheless, at least in a familial high-risk group, the liability to dyslexia extends far more broadly than the categorical diagnosis would imply.

Attention deficit/hyperactivity disorder (ADHD)

Attention deficit/hyperactivity disorder (ADHD), like the other neurodevelopmental disorders, is strongly influenced by genetic factors, shows a marked male preponderance, is associated with specific and general cognitive deficits, and is presumed to have its origins in some form of cognitive processing deficit or bias. Initially, it had been proposed that this deficit involved abnormalities in selective attention but the evidence is against that view. Rather, it seems that the main problem lies in behavioural dysregulation, executive deficits in inhibitory control and working memory, and delay aversion (Castellanos & Tanock, 2002; Sonuga-Barke, 2002). Clinical evidence shows that ADHD poses a distinct clinical problem in many cases by the age of 3 years and pre-school children with ADHD have been found to show both executive dysfunction and delay aversion (Sonuga-Barke, Dalen, & Remington, 2003). Nevertheless, although findings suggest that a liability to ADHD is already present in early life, there are more difficulties diagnosing ADHD in pre-school children than is the case with school-age children.

Numerous studies have shown the high frequency with which ADHD is associated with oppositional/defiant behaviour and conduct problems in childhood. To an important extent this derives from a shared genetic liability but it is uncertain whether or not this constitutes the only mediating mechanism. Follow-up studies have shown that whereas ADHD predicts later antisocial behaviour, the converse does not apply. Nevertheless, there must be caution in drawing causal inferences from this difference because it could simply reflect the usual age of first manifestation of the two different types of behaviour.

The follow-up of clinic samples of children with ADHD into adolescence and adult life has given rise to several important findings (Mannuzza & Klein, 2000; Mannuzza, Klein, & Moulton, 2003). First, adult psychopathology (especially antisocial personality disorder and substance abuse) is more frequent among individuals with ADHD than in comparison samples of young people without childhood psychopathology. Second, although good data are lacking on the extent to which the adult psychopathological outcome is worse for ADHD than other forms of mental disorder in childhood, the findings show that childhood ADHD is the

precursor of later antisocial disorder, even in the absence of co-occurring oppositional defiant or conduct disorder symptoms in childhood (Mannuzza, Klein, Abikoff, & Moulton, 2004). Prognosis is worse, however, for individuals with hyperactivity at school or at both school and home than it is for those with hyperactivity only in the home setting (Mannuzza et al., 2002). Also, it is worse for those who already have associated conduct problems in childhood.

Third, if the standard diagnostic criteria for ADHD are used in adult life, there is a marked drop between adolescence and adulthood in the proportion of individuals who had ADHD in childhood who continue to meet the same diagnostic criteria in adult life. The problem in interpreting this finding is that, when the findings are considered as a whole, it is clear that this does not mean a major improvement in overall functioning; rather, it appears that the particular ways that the malfunction is shown vary with age. The findings from retrospective studies (Kessler et al., 2005a) are broadly similar. Because both the prospective and retrospective studies largely rely on diagnostic categories using similar criteria across the age span, no firm conclusions are possible on the ways in which symptoms may vary with age.

Fourth, both the genetic and epidemiological findings indicate that ADHD features mainly function dimensionally, rather than categorically. As with the other neurodevelopmental disorders, despite marked differences from normal variations, the phenotype extends well beyond traditional diagnostic boundaries. Fifth, although the validity of differentiations among sub-varieties of ADHD lacks a solid empirical base, the evidence suggests that there is valid heterogeneity. Sixth, although the rate of psychopathological, social, and educational impairment in adult life for individuals diagnosed with ADHD in childhood is substantially increased, it is still the case that there is considerable individual variation in outcome and at least half appear to be reasonably well functioning in adult life.

In seeking an understanding of the factors that mediate both the continuities and the discontinuities over time and also the individual differences in developmental course, it will be necessary to take into account the likely importance of both genetic mediators and gene–environment interactions. Thus, using two entirely independent samples, Mill et al. (in press) have shown that polymorphisms in the DRD4 and DAT1 genes were associated with variations in IQ scores within samples of children with ADHD and, furthermore, in the sample that included follow-up into adult life, these same polymorphisms predicted which children with ADHD were at risk for a poor adult prognosis. Thapar et al. (2005) found that a valine/methionine variant in the COMT gene was associated with conduct problems within a sample

of children with ADHD and, moreover, that there was a significant gene-environment interaction between the COMT gene and low birth weight in relation to the association with conduct problems. Both sets of findings are very recent and have still to be replicated by independent research groups using different samples, but the approach is undoubtedly one that is likely to pay off.

Depression

The empirical evidence leaves little doubt that adolescent-onset depression is associated with a strong, specific and direct risk for recurrence in adulthood. Longitudinal data from clinical (Fombonne, Wostear, Cooper, Harrington, & Rutter, 2001; Harrington, Fudge, Rutter, Pickles, & Hill, 1990; Rao, Hammen, & Daley, 1999; Weissman et al., 1999) and community (Bardone, Moffitt, Caspi, Dickson, & Silva, 1996; Fergusson & Woodward, 2002; Lewinsohn, Rohde, Klein, & Seeley, 1999; Pine, Cohen, Gurley, Brook, & Ma, 1998) samples show that 40–70% of depressed adolescents experience a recurrence of major depressive disorder (MDD) in adulthood. Compared with non-depressed controls, depressed adolescents are at 2–7 times increased odds of being depressed as adults. Even after controlling for possible confounding factors such as childhood adversity, IQ, neuroticism, and comorbid diagnoses in a prospective design, the link is significant, suggesting a direct risk association from adolescent to adult MDD (Fergusson & Woodward, 2002). Recent findings indicate that adolescents with subthreshold levels of depression may be no different from adolescents diagnosed with MDD in terms of their risk for adult depression and suicidal ideation, and rates of treatment for depression (Fergusson, Horwood, Ridder, & Beautrais, 2005; Lewinsohn et al., 1999; Pine, Cohen, Cohen, & Brook, 1999). Although a few studies have suggested that stability is greater for females than for males (Costello & Angold, 1995; Ferdinand & Verhulst, 1995), the majority of studies have shown that risk of recurrence is similar for males and females (Fergusson & Woodward, 2002; Harrington et al., 1990; Kovacs, Obrosky, & Sherrill, 2003; Pine et al., 1998; Weissman et al., 1999) despite the significantly higher female-to-male ratio in prevalence rates of MDD, which develops during adolescence. In sum, depression in adolescence tends to signal depression in adulthood.

These patterns of recurrence, however, do not appear to hold for depression that is first manifest before puberty. Harrington and colleagues (1990) first reported the somewhat surprising finding that strong and specific childhood to adulthood continuity of MDD was observed only among individuals with post-pubertal-onset MDD. In contrast, risk for adult MDD in children with prepubertal-onset MDD was no different compared with controls and signi-

ficantly lower compared with post-pubertal-onset cases. Results reported by Weissman and colleagues (1999) mirrored these findings and contributed to the growing notion that childhood-onset and adolescent-onset depression may represent qualitatively distinct disorders (Harrington, Rutter, & Fombonne, 1996). Whether this notion is accurate will depend upon further replication as both studies recruited clinically-referred samples that could bias results. At this point, few long-term longitudinal studies that measure pubertal status are available to help clarify this question and studies investigating age of onset of depression are often inconsistent in defining childhood- vs. adolescent-onset. However, there is good reason to ask whether child-, adolescent-, and adult-onset depression represent one homogeneous disorder. Depressed children and adolescents have been shown to have a different pattern of neurobiological correlates and treatment response to tricyclic antidepressants than do depressed adults (see Kaufman, Martin, King, & Charney, 2001 for a review). Moreover, data from the Dunedin birth cohort study have shown that individuals who were first diagnosed with MDD prior to age 15 years had a significantly different psychosocial risk profile compared with those first diagnosed in adulthood (Jaffee et al., 2002). Whereas the only factor that distinguished adult-onset cases from non-depressed individuals was a history of childhood sexual abuse, juvenile-onset cases were marked by a constellation of early childhood adversity, psychopathology and disruption in their family of origin, and co-occurring behavioural and socio-emotional problems.

Researchers have now begun identifying mechanisms that may mediate the link between early and later depression. First, family history and twin studies suggest the importance of genetic influences. Over a period of over 20 years, Weissman and colleagues (in press) have demonstrated the ongoing nature of the risk for depression (as well as other mental and physical health problems) in the offspring of depressed parents from childhood to adulthood. They have demonstrated that, over three generations of families affected by depression, familial transmission of depression is associated with earlier age of onset, greater risk of recurrence of MDD, and with greater associated impairment, but not with family risk factors. Although this finding points to the possible importance of genetic liability, family studies are unable to disentangle genetic vs. environmental factors that are shared by family members. According to most twin studies, the heritability of depression is low in childhood, it tends to increase in adolescence to a moderate level, and adolescent heritability estimates are fairly stable up to adulthood (Eley & Stevenson, 1999; Silberg et al., 1999; Thapar & McGuffin, 1994). A recent study reported that a higher number of negative life events, which are thought to trigger depression onset, as well as a

greater degree of genetic overlap between negative life events and depression in adolescence than in childhood may explain the increasing heritability estimates across this developmental period (Rice, Harold, & Thapar, 2003). In other words, the rise in the heritability of depression in adolescence appears to be explained in part by an increase in gene-environment correlation (rGE) involving life events.

Second, adverse life experiences in childhood and in adulthood have been shown to increase risk for depression in several ways. To begin with, depressed individuals in both childhood (Rudolph et al., 2000) and adult life (Hammen, 2003) behave in ways that increase the likelihood of interpersonal stressors that can then provoke new episodes or perpetuate continuing depression. Numerous studies have documented the role of both earlier maltreatment in childhood and concurrent stressors in precipitating the first onset of depression, although this has been less apparent in subsequent episodes – a process conceptualised as ‘kindling’ (Kendler, Thornton, & Gardner, 2000; Monroe & Harkness, 2005). The influence of adverse experiences on the risk of depression, however, is also contingent on genetic susceptibility, as shown by the findings on the serotonin transporter gene (Caspi et al., 2003; Rutter, Moffitt, & Caspi, in press). Animal and human studies have also shown that the experience of early adversity can have a lasting impact on reactivity to future stresses (and on vulnerability to depression) via changes in the hypothalamic-pituitary-adrenal (HPA) axis (Boyce & Ellis, 2005), as well as other important neurobiological pathways involved in brain development (Grossman et al., 2003).

Third, there is a long history of research examining the mediating role of cognitive attributional biases in vulnerability to depression (Abramson et al., 2002). Researchers have begun investigating early childhood origins of cognitive vulnerabilities toward depression (Sher, Ingram, & Segal, 2005). Recent studies have shown that as early as 5 years of age, children can have depressogenic cognitive biases, such as a tendency toward negative statements or recall of negative memories (Bishop, Dalgleish, & Yule 2004; Murray, Woolgar, Cooper, & Hipwell, 2001). In children, the experience of depression and a pessimistic explanatory style appear to have bi-directional influences, such that the experience of depression in childhood can lead to a pessimistic explanatory style that persists even after depressive symptoms have remitted, and a pessimistic explanatory style predicts depressive symptoms in late childhood (Nolen-Hoeksema, Girgus, & Seligman, 1992). Cognitive biases that engender vulnerability toward depression are moderately stable over time and likely contribute to the recurrence of depression (Abramson et al., 2002). However, the degree of stability of cognitive vulnerability from childhood to adulthood is unknown.

Sequential comorbidity

Evidence from general population (Kessler et al., 2005b; Pine et al., 1998; Roza, Hofstra, van der Ende, & Verhulst, 2003; Wittchen, Kessler, Pfister, & Lieb, 2000) and high-risk samples (Weissman et al., in press, 2005; Wickramaratne & Weissman, 1998) has shown that anxiety typically first begins in childhood and precedes the onset of adolescent MDD. Moreover, from childhood to early adulthood, the degree of diagnostic overlap has been shown to increase dramatically (Wittchen et al., 2000). This pattern of sequential comorbidity, in which one disorder reliably begins before the other (Angold, Costello, & Erkanli, 1999), has raised the suggestion that anxiety may be viewed as an age-dependent expression of the same underlying disorder as depression (Weissman et al., 2005). Twin studies provide some support for this perspective, as the longitudinal association between childhood anxiety as a precursor to adolescent depression is explained primarily by a common genetic aetiology that might have a different phenotypic expression at different developmental phases (Middeldorp, Cath, van Dyck, & Boomsma, 2005; Rice, van den Bree, & Thapar, 2004; Silberg, Rutter, & Eaves, 2001). In particular, adolescent separation anxiety disorder, generalised anxiety disorder (GAD) and panic are the anxiety disorders that are most likely to develop into adult MDD (Wittchen et al., 2000), and adult MDD is most likely to be preceded by adolescent overanxious disorder (Pine et al., 1998). Nevertheless, some prospective-longitudinal data have shown that adolescent MDD strongly predicts adult anxiety disorders in general (Fergusson & Woodward 2002; Kim-Cohen, Caspi, Moffitt, Harrington, Milne, & Poulton, 2003) and adult generalised anxiety disorder (GAD) in particular (Pine et al., 1998). Moreover, emerging findings from the Dunedin study from age 11 to 32 show that, although up to half of cases of depression in adult life were preceded by prior anxiety, adults with GAD were significantly likely to have had prior MDD in childhood or adolescence (Moffitt et al., in preparation). At least in relation to MDD and GAD, these results contradict the prevailing notion that GAD is a mild early disorder leading toward MDD as a more serious secondary disorder.

Whether the developmental link between anxiety and depression represents the manifestation of two distinct disorders, a single underlying disorder, or a causal association is still in question (see Wittchen, Beesdo, Bittner, & Goodwin, 2003 for a review), and the answers are bound to differ in relation to different anxiety disorders. For now, it appears safe to conclude that in general, anxiety disorders constitute a risk factor for later onset of depression (Wittchen et al., 2000). Emerging clues suggest the possible role of pubertal hormones and increased activity in the hypothalamic-pituitary axis (Walker,

Sabuwalla, & Huot, 2004), as well as increased stressful life events (Silberg et al., 1999) and negative cognitions (Nolen-Hoeksema et al., 1992) that may mediate the developmental link between anxiety and later depression.

Prospective data suggest that there is sometimes a psychopathological progression from substance abuse to major depression, possibly operating through a causal mechanism involving either the psychopharmacological effects of substance abuse on basic physiology or an interference with adequate psychosocial functioning and increased stress generation (Brook, Cohen, & Brook, 1998; Rao, Daley, & Hammen 2000; Stice, Burton, & Shaw, 2004). On the other hand, the reverse progression (i.e., from childhood depression to adult substance abuse) seems much less common, the associations between the two resulting from confounding variables (Fergusson & Woodward, 2002).

Antisocial behaviour

The outcomes of childhood and adolescent conduct problems have substantial homotypic continuity. Most antisocial adults have long histories of behaviour problems reaching back to childhood, but by no means all antisocial children go on to show overt antisocial behaviour later in life (Robins, 1966). Much recent research and theorising has been designed to address this apparent paradox, and to clarify both the roots of heterogeneity in outcomes and the mechanisms that contribute to persistence and desistance over time. In addition, numerous studies have confirmed that a focus on homotypic continuities in antisocial behaviour alone is too narrow: early conduct problems can markedly compromise social and relationship functioning in adulthood (Zoccolillo, Pickles, Quinton, & Rutter, 1992), and have implications for both physical (Laub & Vaillant, 2000) and mental health (Kim-Cohen et al., 2003).

Heterogeneity in outcomes

Probably the most dominant recent model for understanding variability in later outcomes has been Moffitt's (1993) developmental taxonomy. This proposed that the total 'pool' of antisocial youth is made up of two relatively distinct sub-groups, differing in both early risks and long-term outcomes, and distinguished by age at onset. The poorest outcomes are to be expected for the relatively low prevalence, male-dominated forms of antisocial behaviour that begin early in childhood, and are associated with both neurodevelopmental difficulties (neuropsychological deficits, difficult temperament, or hyperactivity) and adverse rearing conditions. Adolescent-onset delinquency, by contrast, is viewed as largely normative – the product less of individual risks than of frustrations attendant on the adolescent 'maturity gap', and

social mimicry of deviant peers. As follows from this account, persistence in antisocial activities is not expected in this group once young people take on the responsibilities and reap the benefits of involvement in adult roles.

This model has proved a powerful organising framework, and generated extensive research. In the main, key postulates of the theory have been supported (Moffitt, in press), though some modifications may be warranted, and some unexpected findings have emerged. Importantly, the poor long-term prognosis for early-onset disruptive behaviours has been repeatedly confirmed. Modest associations with risk for later antisocial outcomes have been detected in temperamental characteristics assessed as early as age 3 (Caspi, Moffitt, Newman, & Silva, 1996), and prospective follow-ups from middle-late childhood have documented the pervasiveness of the later difficulties involved. Fergusson, Horwood, and Ridder (2004), for example, found that conduct problems at ages 7–9 years were associated with increased risk for antisocial personality disorder and crime in early adulthood (ages 21–25 years), but also with poor educational and occupational achievements, adverse sexual and partner relationships (including domestic violence), early parenthood, and increased risks of substance use, mood and anxiety disorders and suicidal acts. With the exception of educational and occupational problems (primarily attributable to correlated childhood risks), links with all other outcomes were robust to controls for an array of individual and social background confounds, and were linearly associated across the range of severity of early conduct problems, rather than concentrated in extreme high scoring or diagnostic groups. Though both levels of conduct problems and later outcomes differed for boys and girls, long-term consequences were essentially similar for young people of both sexes.

Studies have also shown, however, that not all early-onset conduct problems persist in that form. A small proportion with marked early disruptiveness go on to show good adaptation in adulthood; little is known as yet of the protective factors that enable these constructive outcomes. More unexpectedly, several studies have now identified a sub-group with early-onset difficulties whose prognosis is also poor, but where later difficulties are of a quite different kind, marked by social isolation, avoidance of close relationships, and vulnerability to anxiety and depressed mood (Moffitt, in press). Though data on such groups are sparse, two important features are beginning to emerge. First, boys on such 'childhood-limited' pathways show histories of early psychosocial adversity and neuropsychological deficits quite as severe as those whose antisocial tendencies persist (Raine et al., 2005). Second, 'avoidant' outcomes of this kind may be quite as common sequelae of early childhood disruptiveness as

persistence in overtly antisocial traits. If confirmed, these findings suggest that though early onset of behaviour problems may indeed be a key marker for poor later adjustment, other features – as yet unrecognised – must be implicated in determining their form.

Findings on adolescent-onset groups have also suggested some modifications to initial expectations. In terms of later outcomes, the few follow-ups of well-defined adolescent-onset groups have shown a less benign course than initially anticipated, at least into the mid-20s; though outcomes are less adverse than for early-onset groups (and in particular show less evidence of violent offending or aggression in interpersonal relationships), rates of property crime remain elevated, and risks of substance use and mental health problems are also increased (Moffitt, *in press*). It is unclear at this stage whether this reflects the more extended ‘timetable’ for achieving independent adult status experienced in recent cohorts, or whether even relatively short-term involvement in adolescent delinquency results in risks for later functioning.

Mechanisms for persistence and desistance

Pervasive disruptive behaviours are highly heritable (Arseneault et al., 2003); genetically based liabilities are thus likely to play a key part in both the onset and persistence of early-onset conduct problems. Much evidence also, however, points to a role for environmental influences, and the likelihood of gene–environment interplay (Rutter et al., *in press*; Rutter & Silberg, 2002). In some instances, genetic factors may moderate vulnerability to environmental adversity: replicated findings have now shown, for example, that variations in the *MAOA* genotype moderate vulnerability to maltreatment and other environmental correlates of conduct problems (Caspi et al., 2002). In addition, gene–environment correlations and interactions are likely to be implicated, with children’s heritable traits both evoking negative reactions from others and contributing to the selection of environments likely to reinforce existing patterns of behaviour. In childhood and adolescence, deviant peer affiliations seem central to such effects (Fergusson, Swain-Campbell, & Horwood, 2002); later in adolescence, partner choices appear to function in similar ways (Woodward, Fergusson, & Horwood, 2002). Over time, cumulating transactions of this kind with successive interactional partners are assumed to stabilise early difficulties through a variety of processes: direct reinforcement of maladaptive behaviours and interactional styles; effects on self and social cognitions; and reduced opportunities for involvement in more adaptive styles of functioning. In addition, conduct problems have consistently been associated with ‘precocious’ patterns of adolescent and early adult role transitions – early exits

from education, and early entry into sexual relationships and parenting – which, along with increased risks for substance use, contribute further to compromising life chances and increasing exposure to stress (see Maughan & Rutter, 2001 for a more detailed discussion).

Cumulating consequences of this kind, often described in terms of indirect chains or cascades of risk (Masten et al., 2005), seem likely to constitute key mechanisms in the persistence and elaboration of early-onset conduct problems. Although routes for the persistence of adolescent-onset difficulties have been less studied to date, many are likely to be similar: deviant peer influences, truncated educational opportunities and involvement in substance abuse seem likely to form at least part of the story. What is unclear at this stage, however, is whether age at onset *per se* contributes to variations in persistence or intervening mechanisms, or whether its primary role is as a marker for variations in liability to other individual or environmental risks. Whereas it seems possible, for example, that the high risks associated with childhood onset largely reflect effects of associated hyperactivity, neuropsychological deficits and aggression, it is also plausible that longer exposure to the cumulating consequences of behaviour problems carries some independent effects, especially on styles of relationships, personality functioning and cognitions. As yet, the key tests needed to answer these questions have still to be carried out.

Finally, differing sub-groups of antisocial youth may vary in their exposure to, and ability to profit from, experiences later in development associated with desistance from antisocial behaviour and crime (Laub & Sampson, 2001, 2003). Although the great majority of offenders desist eventually, a range of evidence points to the existence of ‘turning point’ experiences in early adulthood that speed recovery and signal more radical changes in trajectories. Certain core characteristics have been identified: turning points are associated with experiences that provide clear separations of the present from the past; opportunities for investment in new relationships offering support, and access to new social networks; formal or informal forms of supervision and monitoring of behaviour; structured activities; and opportunities for identity transformation. In some cases such experiences arise through relatively rare events, such as involvement in military service. Increasingly, however, studies have centred on the effects of more common experiences – in particular the roles of supportive marriages and positive work involvements – in promoting desistance from crime. Importantly, evidence suggests that effects of such experiences are robust to selection processes, and open to reversal if positive relationships come to an end (Laub & Sampson, 2001, 2003).

Risks for psychiatric disorder in adult life

In addition to continuities in antisocial behaviour and poor social functioning, childhood and adolescent conduct problems are strongly associated with an increased risk for psychiatric disorder later in life. Follow-back findings from the Dunedin study, for example, showed that – unique among childhood disorders – conduct problems at ages 11–15 were associated with increased risk for all psychiatric disorders at age 26, including internalising problems, schizophreniform disorders and mania, as well as broadly externalising phenomena such as substance abuse (Kim-Cohen et al., 2003). As yet, the basis for many of these vulnerabilities remains unknown. Associations with substance use and depression have, however, received considerable attention. Conduct problems are strong predictors of adolescent substance use; independent of these selection effects, both alcohol and cannabis use early in adolescence predict later conduct problems and delinquency. As outlined below, risks for substance use typically vary with stage of involvement (initiation, frequent use, abuse and dependency), with genetic effects more marked for later stages in this progression. Consistent with this pattern, though conduct problems are associated with increased risk for all stages of substance use, risk mechanisms appear to vary by age and stage. Twin studies have shown, for example, that at age 14, when symptoms of alcohol dependence are rare, associations with conduct problems are entirely attributable to shared environmental influences (Rose, Dick, Viken, Pulkkinen, & Kaprio, 2004). By age 17, by contrast, all the covariation between antisocial symptoms and alcohol dependence in males appears due to a shared genetic liability (Malone, Taylor, Marmorstein, McGue, & Iacono, 2004), noted in other studies to be associated with personality characteristics of impulsiveness, risk-taking and lack of behavioural restraint (Krueger et al., 2002). In addition, Malone et al. (2004) found evidence that alcohol dependence at age 17 had effects on antisocial symptoms at age 20, confirming other reports that alcohol involvement in adolescence may ‘ensnare’ otherwise desisting young men into more persistent antisocial behaviour. A variety of mechanisms may be involved here, ranging from the disinhibiting effects of substance use through peer influences, adverse effects on family relationships, and the need for money to support alcohol or drug habits.

Associations with depression highlight different issues. Early-onset depression is strongly associated with conduct problems; the most common pattern being for conduct problems to precede the expression of affective symptomatology. By the teens, rates of comorbidity between depression and conduct/oppositional defiant disorders are high (Angold et al., 1999); by the early 20s, findings from the Dunedin study (Moffitt, Caspi, Rutter, & Silva, 2001) showed

that almost three-quarters of girls with adolescent conduct disorder had experienced an episode of depression. Although such associations can be expected to attenuate with age, a history of adolescent conduct problems remained associated with increased risk for depression for both males and females in that same sample at age 26 (Kim-Cohen et al., 2003).

The precise mechanisms underlying these associations remain to be established. Some commentators (e.g., Zoccolillo, 1992) have argued that conduct disorder is a problem of multiple dysfunction, intrinsically involving both behavioural and emotional dysregulation. In part, shared liabilities are likely to be implicated, with studies in adolescence finding evidence for both shared environmental (Fergusson, Lynskey, & Horwood, 1996) and genetic risks (O’Connor, Neiderhiser, Reiss, Hetherington, & Plomin, 1998). How far this accounts for longer-term prediction is unknown; other evidence suggests that conduct problems select individuals into environments likely to be marked by high rates of stress (Champion, Goodall, & Rutter, 1995), and exposure to failures in relationships and academic settings may contribute to the development of depressogenic cognitions. Further research is needed to clarify the relative roles of these varying processes at different stages of the life-course, and to determine whether longitudinal associations between antisocial behaviour and depression are best conceived of in terms of heterotypic continuities in a shared underlying vulnerability, or as psychopathological progressions between distinct disorders.

Substance abuse

Epidemiologic studies have consistently confirmed that, although the majority of young people experiment with recreational drug use in their mid-late teens, progression to abuse or dependence is much less common (Fergusson & Horwood, 2000; Kandel, Yamaguchi, & Chen, 1992). Risks for these different stages of involvement in substance use vary, and increasing evidence suggests that associations with other disorders also reflect differing patterns of effects at different stages in development.

Some of the main associations with prior childhood disorders have been highlighted in earlier sections. Of these, childhood and adolescent conduct disorder show the strongest links, being associated with both early initiation and progression in a range of types of substance use. As outlined above, mechanisms underlying these associations vary with age and with stage of involvement; in addition, later adolescent substance abuse has reciprocal effects in increasing risk for persistence in crime. Rates of later substance abuse are also elevated in ADHD samples, though effects here may largely be mediated via associated conduct problems. Links with depression

are more complex. Depressed mood is strongly associated with use of a range of substances in both adolescence and adulthood; in general, these links have been assumed to reflect efforts at self-medication. Longitudinal evidence, however, casts doubt on this interpretation, at least in adolescence: studies of teenage cannabis use, for example, find no evidence of direct effects of depressive symptomatology (Rey et al., 2004), and follow-ups of depressed samples show little evidence of increased rates of later alcohol or other drug abuse (see, e.g., Fombonne et al., 2001). Prediction from substance use to later depression is, however, strong (Rao et al., 2000), and longitudinal studies of drug abusers highlight the increased physical and psychopathological risks – including both completed suicide and accidental deaths – that can follow from teenage substance use (see, e.g., Brook et al., 1998). As we have seen, early cannabis use – once thought to hold few deleterious consequences – is now known to form part of the risk pathway for schizophrenia in some vulnerable individuals; and models of cannabis as a ‘gateway’ to harder drug use have now been confirmed in a number of prospective investigations (see, e.g., Fergusson & Horwood, 2000).

Adolescent substance use is associated with a broad spectrum of risks, both heritable and psychosocial. Many of the psychosocial risks identified reflect early family-based adversities that overlap with risks for other childhood disorders, leaving it uncertain how far effects are specific to drug-related problems or operate primarily via effects on other disorders. In general, genetic effects are stronger for abuse and dependence than for initiation and recreational drug use, where shared environmental influences predominate. Rhee et al. (2003), for example, found twin-specific environmental influences on tobacco initiation, alcohol use and any drug use in adolescence, pointing to the likely importance of variations in availability and peer influences on early stages of substance involvement. This interpretation finds strong echoes in longitudinal studies, where adolescent peer affiliations have been shown to have independent influences on substance use after controls for selection effects, including prior individual characteristics (Fergusson et al., 2002). In addition, shared genetic influences may also contribute to comorbidity with other disorders; thus, all of the covariation between antisocial behaviour and alcohol dependence in the late teens appears attributable to effects of this kind, and shared genetic liabilities have also been reported between substance use and depression in adolescence. It remains to be seen how far associations with other disorders, and with specific substances, show similar patterns of effects.

Finally, mention must be made of age at onset of substance use as a potential predictor of adverse later outcomes. From the time of the first large-scale epidemiologic studies, early initiation in substance use – typically before the mid-teens – has been noted

as a strong marker for both progression in substance-related pathways and more global difficulties in later functioning. As with antisocial disorders, these findings raise key questions about the nature of the effects involved: does early initiation itself contribute directly to later risk, or does it serve primarily as a marker for a more severe, and possibly generalised, liability to subsequent psychopathology? McGue and Iacono (2005), examining a range of adolescent problem behaviours (including delinquency and early sexual behaviour as well as alcohol and drug use), found strong evidence for a generalised risk for early-onset problems (before age 15), with mean correlations between indicators of .55 in males and .64 in females. Young people with multiple indicators of early problem involvement, encompassing both drug and alcohol use and other difficulties, showed exceptionally high rates of both externalising disorders and depression at age 20. This suggests that factors (genetic and environmental) underlying a general tendency to early adolescent problem behaviours, rather than specific to individual aspects of early psychopathology, may be key to understanding later risks.

Overarching themes

Heterotypic continuity and psychopathological progression

Earlier sections of this review provided several instances in which behaviour of one type at an early age is predictive of behaviour of an apparently different type at a later age. The two concepts that have mainly been used to encapsulate this phenomenon are ‘heterotypic continuity’ and ‘psychopathological progression’. Two rather different notions underlie these terms. First, there is the postulate that there is meaningful continuity in the course of a particular disorder but that the ways in which it is manifest change with increasing age. Examples include the connections between reading difficulties in childhood and spelling problems in adult life; between neurodevelopmental impairment in early childhood, psychotic-like features in middle childhood, and frank psychosis in late adolescence/early adult life in the case of schizophrenia; and between early anxiety and later depressive disorders. In each of these cases, the usual assumption has been that there has been no change in the disorder as such, even though the particular behavioural features are not identical at different ages.

In some cases there is obvious continuity in the impairments that are evident; that would be the case, for example, with early reading and later spelling. Both of these features reflect different aspects of written language. Not surprisingly, therefore, the continuity is very high between childhood and adult life. The same, albeit to a lesser degree, probably also applies to connections between

prepubertal anxiety and post-pubertal depression. In this case, however, the progression raises the query as to why anxiety has been transformed into depression. Is there something specific to the adolescent age period that has predisposed to that occurrence? Anxiety and depression commonly co-occur at all ages. That is to say, the progression from anxiety to depression also applies in adult life. However, there is not invariance in the order of these features (i.e., depression may precede, as well as follow anxiety). In other words, although during adolescence the usual order is from early anxiety to later depression, in other age periods the order can go in the opposite direction.

The situation is somewhat different with respect to schizophrenia, if only because the connections over time are much weaker. Impairments in receptive language in early childhood and in early motor development are by no means specific to schizophrenia. Most children showing these features do not become schizophrenic. There is relative diagnostic specificity with respect to the association with schizophrenia rather than with other mental disorders in adult life but the rate of the childhood precursors is far higher than the rate of the adult outcome of schizophrenia. The same applies to the psychotic-like features in middle childhood and the so-called prodromata occurring in late adolescence. The precursors and prodromata are both much commoner than schizophrenia and it remains to be established what causal process underlies the transition from one to the other. All these examples would generally be incorporated within the concept of heterotypic continuity but it needs to be emphasised that that is a descriptor and not an explanation. In each case, the mediating mechanisms have to be identified and probably they will not be the same in each of the examples.

It is not as yet clear whether the progression from specific language impairment in early childhood and widespread social impairment in adult life falls within the concept. There is no reason to suppose that the social difficulties in adult life represent a different disorder that has arisen anew. Rather, the implication is that the starting concept of a 'pure' language disorder was probably mistaken. Although a delay in the development of speech and an understanding of spoken language constitute the identifying starting point, the basic disorder almost certainly includes a broader cognitive deficit that includes social cognition as one of its facets. If that is accepted, then 'heterotypic continuity' is probably an appropriate descriptor. In other words, the disorder has remained the same but its manifestations have altered. The adults who had shown language delay in early childhood would no longer be easily identified as having a language disorder despite the fact that detailed testing shows that their language functioning is still impaired, albeit in a more subtle fashion. Rather, they mainly stand out through their social malfunction.

Other examples, probably better conceptualised as psychopathological progressions, seem to be rather different in that it is not self-evident that the later behavioural features represent the same disorder as the earlier ones. Thus, for example, although the progression from early conduct disturbance to later substance misuse may well represent different manifestations of the same underlying construct of disinhibited or risk-taking behaviour, it is less clear whether the transition from substance abuse to depression can be seen in the same way. Rather, it seems more likely that the pharmacological effects of substance use create an increased risk for depression. Similar questions arise with respect to the progression from ADHD to a later antisocial personality disorder. Longitudinal studies show that this is unidirectional (that is to say early conduct disturbance does not create a risk for the later emergence of ADHD). Cross-sectional data indicate that ADHD and antisocial behaviour involve a substantial degree of shared genetic liability. Nevertheless, the meaning is still not entirely clear. Is the form of antisocial behaviour that is associated with ADHD meaningfully different from other varieties of antisocial behaviour? Or, does the behaviour of impulsiveness/inattention/hyperactivity create an environmentally mediated risk for antisocial behaviour?

Early age at onset

Similar questions about mediating mechanisms apply to the phenomenon of the increased risks for later psychopathology that have often been observed in relation to an unusually early age at which a particular form of psychopathology is evident. It has often been assumed that the early age is itself a direct causal factor. In other words, if people could be persuaded to take actions to delay particular behaviours this would prevent later adverse outcomes. The discussion of findings with respect to substance abuse indicates no such assumption should be made without testing alternative explanations. The same applies to the increased risk effects for antisocial behaviour persisting into adult life associated with an unusually early onset of conduct problems. The question here is whether the mechanism lies in the association with ADHD, rather than the age of onset as such. That is, is the worse onset simply a function of associated ADHD, there being no such similar risk effect for early manifestations of conduct problems that are not accompanied by ADHD? Once more, the data to decide between these alternatives are not adequately available but the implication is that research attention must focus on the delineation of the mediating mechanisms before the causal inferences can be made.

Similar questions arise with respect to the unusually early onset of depression. In this case, the

early onset is not associated with a worse long-term outcome. Rather, it is associated with a somewhat different set of correlates. The lack of clarity in this case concerns the differentiation between implications that the nature of the depressive disorder differs by age of onset, as against the possibility that the different correlates instead reflect circumstances in childhood that colour the clinical picture associated with depression, but do not have implications of a different meaning. Much of the research has focused on a pre- and post-pubertal contrast, but uncertainty remains on the extent to which the differentiation is a function of chronological age or puberty. Similar questions need to be asked with respect to the findings that heavy use of cannabis in adolescence constitutes a risk factor for schizophrenia, whereas comparable use in adult life does not.

Mediators of continuities and discontinuities in psychopathology

In considering the mechanisms that might mediate continuities and discontinuities in psychopathology between childhood and adult life, some half a dozen different possibilities need to be considered. First, it is likely that genetic liabilities will be influential. Thus, with respect to depression, recurrence is more likely when there is a heavy familial loading (although this may reflect environmental as well as genetic influences). But it should not be thought that there will be a deterministic genetic influence on persistence. Thus, the evidence of important gene-environment interactions in the fields of antisocial behaviour, depression and schizophrenia all indicate that the genetic effect operates in part on susceptibility to environmental hazards (Rutter et al., in press).

Second, so-called kindling effects may be important; the postulate being that the experience of a mental disorder brings about changes that make recurrence more likely. Monroe and Harkness (2005), however, have pointed out that the empirical evidence that the associations between major stressors and the onset of depression are weaker for recurrences than for first episodes could mean either that a kindling effect *reduces* sensitivity to major stressors, or that it *increases* stress-sensitivity so that minor events trigger onset without the need for a major negative life event. Research is needed to test these contrasting alternatives. At least with respect to schizophrenia, and possibly also depression, there is some suggestion that effective early treatment may improve prognosis and, conversely, that a prolonged period without treatment may make the outlook worse.

Third, as discussed in relation to antisocial behaviour, there is good evidence from long-term longitudinal studies that antisocial psychopathology increases the likelihood of exposure to risk environments in adult life. Fourth, however brought about, adverse experiences in childhood (such as exempli-

fied by physical and sexual abuse) and in adult life (as exemplified by life stresses carrying long-term threat) may influence the likelihood of occurrence of depressive disorders (and possibly other forms of psychopathology) in adult life. That is, there may be long-term sequelae of early experiences and, in addition, later experiences may foster recurrence. Fifth, the ways in which individuals respond to their psychopathology are likely either to increase or to decrease later risks. For example, a reliance on drugs or alcohol to relieve depression is a coping strategy that brings its own psychopathological risks. Sixth, there are indications that how people conceptualise what is happening to them influences the course of the psychopathology from which they are suffering. This has been written about most extensively in the field of depressive disorders but the negative aspects of attributional biases constitute the basis of the cognitive behavioural treatment of a very much broader range of disorders.

How early in life is behaviour predictive of later psychopathology?

The predictive power of early behaviour needs to be considered from two rather different perspectives. First, there is the question of whether or not the later psychopathology involves abnormalities that are present at a very early age. The second question is whether or not such abnormalities can be measured in a manner that is sufficiently reliable and valid to provide prediction that is useful at the individual level. Autism well illustrates the need to make that distinction. There are good reasons for supposing that autism is present from early infancy onwards and that this is sometimes observable – as shown, for example, by the analysis of home movies. On the other hand, the evidence shows that diagnosis becomes secure only after about the age of two years and that many cases are missed by assessments below the age of eighteen months. The findings with respect to specific language impairment and dyslexia tell a similar story. Early assessments can, and sometimes do, show abnormalities at a very early age but the diagnosis becomes secure only several years later. Although research into the connections between functioning in infancy and later psychopathology is important, there must be considerable caution about the value of early interventions based on infancy features. False negatives and false positives will be very frequent. Accordingly, the risks to the many have to be balanced against the possible benefits for the few.

Theoretical perspectives on developmental pathways

Finally, we need to consider whether theoretical cohesion is currently possible on the principles and

mediating mechanisms involved in continuities and discontinuities in psychopathology between childhood and adult life. Several of the leaders of long-term longitudinal studies have presented models (Laub & Sampson, 2003; Masten, Obradović, & Burt, *in press*; Moffitt, *in press*; Pulkkinen, Feldt, & Kokko, 2005; Pulkkinen, Kaprio, & Rose, *in press*; Sroufe, Egeland, Carlson, & Collins, 2005; Steinberg et al., *in press*; Werner & Smith, 2001). There are important areas of agreement in their conclusions, all of which are borne out by the findings we have reviewed. Thus, development necessarily includes continuity and change, with both involving coherence, lawfulness and organisation. There is an ongoing person–environment interplay, with the early years influential through the lasting chain effects that may be set in motion. Individual differences are marked and there are multiple converging and diverging causal pathways. Continuities between normality and psychopathology are extensive.

Nevertheless, there are also important differences in emphasis in the models put forward. Thus, Laub & Sampson (2003) and Werner and Smith (2001) are distinctive in stressing the importance of turning-point experiences in adult life, although these also play a part in Masten et al.'s (*in press*) model. Empirical findings support their views. They note, however, that such experiences are not random because people's own behaviour and experiences shape their later experiences. Also, although experiences that open up opportunities are crucial, how people use such opportunities is equally influential.

Sroufe et al. (2005) proposed that the key feature concerns the organisation of early attachment relationships; Moffitt (*in press*) placed greater emphasis on neurodevelopmental features, and Steinberg et al. (*in press*) pointed to the likely importance of biological changes during puberty (noting, however, that they are embedded in the social context). Curiously, genetic factors do not occupy a major position in any of the models, other than that put forward by Pulkkinen et al. (*in press*), although they are acknowledged in most models and given some importance by Moffitt (*in press*). The research findings strongly suggest that much specific attention will need to be paid to genetic mechanisms, but they also emphasise that many will operate through influences on gene–environment interplay rather than through direct effects on psychopathology (Rutter et al., *in press*).

Most of the models note the importance of personal agency, what people do in response to the challenges they face. Similarly, emphasis has been placed on the mediating role of emotional and behavioural regulation (Pulkkinen et al., *in press*). It is reasonable to suppose that both may influence either continuity or change in psychopathology, but there has been only limited testing of mediation through coping strategies or mental sets.

Sroufe et al. (2005) stand out with respect to their claim that almost all psychopathology involves continuity with normality and that psychiatric diagnosis is of very limited value. The research findings we have reviewed provide ample evidence of the uncertainties regarding diagnostic boundaries, and of the extent to which risk and protective processes for different disorders have much in common. Nevertheless, as the examples of disorders we have considered illustrate, diagnostic differences are important.

In conclusion, long-term prospective longitudinal studies have been hugely informative in showing the findings on continuities and discontinuities in psychopathology that have to be understood. Moreover, there has been real progress in recognising the need to test alternative hypotheses on mediation, and in beginning to undertake such tests. The findings do not allow an all-encompassing model but they do indicate that research should be able to identify mediating processes and that lawful principles should be found even if it is unlikely that one theoretical model will be adequate.

Future directions

Although much has been achieved in studying continuities and discontinuities in psychopathology, between childhood and adult life, major challenges remain. As we have emphasised throughout, there needs to be a focus on competing alternatives with respect to mediating mechanisms, and this requires attention to measurement, research design and data analysis. There is a particular need to determine the factors involved in changes during adolescence (in relation to the rise in rate and changing sex ratio of depressive disorders, the transition from prodromal phase to overt psychosis in schizophrenia, and the emergence of adolescence-limited antisocial behaviour – to mention but three examples). It will be important to measure potential transitions as well as age, and biological features will need to be studied in their social context. Basic research into brain development during adolescence is needed, but this will need to incorporate investigation of individual differences and their implications for psychological functioning. Up to now, rather limited use has been made of genetic designs (either quantitative or molecular) and they will need to be employed more widely in order to test mediating mechanisms, both genetic and environmental. Cognitive processing of experiences has been much emphasised in developmental theorising, as have relationship qualities and capacities. In both cases, however, much more rigorous testing of their postulated mediating role in psychopathological development is required. The key message, however, is that the concepts and methodologies are available for the successful meeting of these challenges.

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