CHAPTER 1

Development and psychopathology: a life course perspective

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Introduction

A life course perspective is central to developmental psychopathology. Michael Rutter and Alan Sroufe, founding fathers of the discipline, argued this need from the outset (Sroufe & Rutter, 1984; Rutter & Sroufe, 2000), and the intervening decades have amply confirmed their view. Longitudinal research has consistently demonstrated that most adult disorders have roots in childhood difficulties, and most childhood disorders have sequelae that persist to adult life. In mapping these long-term linkages, developmental findings have challenged etiological assumptions, highlighted unexpected connections across the life course, and raised key questions about the mechanisms—biological, psychological, and social—that underlie continuity and change.

Numerous insights have flowed from adopting a life course view. It is now clear, for example, that the burden of psychiatric disorders begins early in development. Disorder onsets fall into distinctive groupings (Angold & Egger, 2007), but most occur in childhood and adolescence. Some—such as the neurodevelopmental disorders—emerge very early in childhood; some—such as depression—show a sharp rise in the teens; and some—schizophrenia being the most obvious example—though typically emerging later in development have clear precursors in the childhood years. These differing onset profiles point to differences in underlying mechanisms. Developmental neuroscience is beginning to map the delays and perturbations in brain development characteristic of specific childhood disorders (Shaw *et al.*, 2010); to clarify the effects of stress exposure at different stages in the life course (Lupien *et al.*, 2009); and to highlight how both the pre- and postnatal environments affect epigenetic programming, with the potential for pervasive influences on the developing brain (Kofink *et al.*, 2013).

Long-term studies have also documented the strikingly high cumulative prevalence of mental health problems in the first two decades of life. Cross-sectional surveys identify around 10–12% of young people as disordered at any particular point in time; repeated longitudinal assessments, by contrast, suggest that well over 50% of young people will meet criteria for at least one psychiatric disorder by age 21 (see e.g. Copeland *et al.*, 2011). Looking backwards from adulthood, early vulnerability to adult disorder is equally clear; one follow-back study found that half of those with treated mental health problems in early adulthood had first met criteria for disorder by age 15 (Kim-Cohen *et al.*, 2003). Underlying these general linkages, developmental findings reveal a complex mix of continuities and discontinuities, and evidence of both *homotypic* prediction—the persistence or recurrence of the same disorder in different developmental periods—and apparently *heterotypic* transitions, where earlier and later vulnerabilities differ in form. Early emotional and behavioral difficulties also foreshadow a broad spectrum of problems in adult social functioning; poor physical health and health-related behaviors; poor economic circumstances (Goodman *et al.*, 2011); and, in some instances at least, an increased risk of early death (Jokela *et al.*, 2009).

Identifying the processes that underlie these differing pathways is central to the developmental psychopathology approach (Sroufe & Rutter, 1984). This chapter draws together evidence of this kind, using findings on selected disorders and early risks to highlight current issues in the field. Because tracing long-term developmental linkages poses particular methodological challenges, we begin with a brief overview of methodological issues, highlighting the strengths and limitations of differing research designs in identifying life course pathways, and the new techniques now available to investigators to delineate developmental mechanisms in longitudinal research.

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Methodological considerations

Research designs

Optimal research designs vary with the question of interest. Robins' classic study of child guidance patients (Robins, 1966) is a landmark example of a "catch-up" study, designed to examine long-term outcomes of childhood conduct problems. Identifying her sample from child guidance records, Robins traced and interviewed prior clinic attenders in adulthood, gaining a broad picture of strengths as well as difficulties in their later lives. She used a general population sample from the same geographical area as a comparison group, and also paid attention to differences in outcomes within the treated group. The findings proved hugely influential: diagnostic criteria for Antisocial Personality Disorder were largely shaped by her findings, and the study generated numerous other developmental hypotheses that have stood the test of time.

Prospective studies of non-referred samples provide for a variety of extensions to this approach. First, they can include research-based assessments from the outset, allowing more nuanced tests of the early features most important in influencing later outcomes. Second, because they can include multiple assessment waves, they allow better tests of the timing and patterning of difficulties as they unfold over time. And third, they offer better opportunities to test hypotheses about possible causal mechanisms. Numerous studies have now used strategies of this kind; to take just one example, Laub and Sampson's (2003) long-term follow-up (to age 70) of the Gluecks' juvenile delinquency sample has been especially informative on the role of adult experiences, showing how both negative and positive experiences continue to shape developmental trajectories well into adult life.

Prospective studies of non-referred, population-based cohorts share many of these advantages, but have additional strengths: they are unaffected by referral biases; they can examine effects of environmental risk exposures; and they can also be used to study outcomes of dimensionally-defined behaviors or traits. Follow-back analyses tracing the childhood histories of individuals with particular later outcomes can also be derived from epidemiological/longitudinal data. Alongside these strengths, there are, of course, potential limitations. Some level of attrition is almost inevitable in long-term follow-ups, and may affect the representativeness of the retained samples; in addition, changes in diagnostic criteria may mean that study definitions devised in one era do not map precisely to more recent conceptualizations of disorder. The strengths of this design are, however, well attested by the extensive insights that continue to emerge from key epidemiological/longitudinal studies, including the Dunedin (http://dunedinstudy.otago.ac.nz/) and Christchurch (http://www.otago.ac.nz/christchurch/research/healthdevelopment/) studies in New Zealand, the Great Smoky Mountains Study in the United States (http://devepi.duhs.duke.edu/gsms.html/) and the Avon Longitudinal Study of Parents and Children (ALSPAC) in the United Kingdom (http://www.bristol.ac.uk/alspac). Biomarkers are now frequently collected in longitudinal studies of this kind; prenatal influences are being investigated in studies beginning in pregnancy; and longitudinal twin studies are increasingly being used to document stability and change in genetic influences across development.

For some research questions, other designs are valuable. Studies of the very early precursors of disorder, for example, can capitalize on high-risk designs, tracking children selected on the basis of family or genetic risk. Lyytinen *et al.*'s (2008) prospective study of babies in families with dyslexia, for example, obtained detailed cognitive and neurophysiological measures from very early in development, identifying hypothesized precursor deficits well before children were exposed to the demands of learning to read. High-risk designs can also be used to assess long-term outcomes of early adversities such as maltreatment or early institutional deprivation, allowing both for tests of environmental risk mediation and contributors to variations in outcome within high risk groups.

Retrospective and prospective measures

In general, "prospective," contemporaneous measures of childhood behaviors or experiences are almost always preferable to retrospective reports of childhood collected in adult life. People are much better at remembering *whether* something happened than exactly *when* it occurred, and memories of the temporal ordering of events or behaviors—often required to test causal hypotheses—are especially open to bias. Retrospective reports of the age of onset of anxiety disorders, for example, seem heavily influenced by the age at which respondents are questioned (Beesdo *et al.*, 2009), and estimates of the lifetime prevalence of a number of common disorders are markedly higher when calculated from prospective rather than retrospective reports (Moffitt *et al.*, 2010). For memorable, easily defined events such as parental divorce or the timing of menarche, retrospective recall seems unlikely to be problematic (Hardt & Rutter, 2004). Deliberate falsifications are probably uncommon, and the main source of bias seems to arise from individuals who are functioning well in adulthood forgetting or underreporting early risk exposures, rather than those with poor outcomes exaggerating early adversities. Some events—such as early exposure to sexual or physical abuse—cannot usually be assessed in non-referred samples in childhood on ethical grounds, so much of what we know about their long-term implications is inevitably based on retrospective reports. Where comparisons with prospective data have been feasible, some have found very similar associations with risk for later disorder (Scott *et al.*, 2012), while others have not (Widom *et al.*, 2007); other evidence suggests that measurement errors in retrospective reports of child maltreatment have a quite limited influence on associations with later mental health (Fergusson *et al.*, 2011). As a result, although prospective data are to be preferred whenever feasible, it is

important not to exaggerate the problems of retrospective reporting, and to appreciate that there are circumstances where it is the only strategy realistically available. Finally, it is of course worth remembering that most "prospective" studies actually involve an element of retrospective reporting, reflecting events or behaviors occurring between study assessments.

Statistical methods for longitudinal research

Many long-term studies now include multiple assessments spanning long periods of the life course. To optimize the value of these rich resources, a range of specific statistical techniques has been developed (see Chapter 15). Some (such as multiple imputation) are designed to deal with problems of attrition; some (such as latent variable models) provide approaches to handling the complexity of both environmental and genetic risks for child mental health; and some (including structural equation modeling and cross-lagged panel analyses) provide tests of hypothesized mediating mechanisms and bidirectional effects. Arguably the most prominent recent developments, however, are methods that explicitly model patterns of stability and change over development, including group-based trajectory modeling, used to identify sub groups within the population that differ in their developmental course (Nagin & Odgers, 2010). First widely used in longitudinal studies of antisocial behavior, group-based modeling of this kind has since been applied to a wide range of phenomena, from pathways in early reading development (Lyytinen *et al.*, 2006) to trajectories of common mental health symptoms across the life course (Colman *et al.*, 2007). Trajectory modeling provides a direct means of testing etiological influences on sub groups with distinct developmental profiles, and can also be used to evaluate variations in intervention response.

Childhood–adulthood continuities

We turn now to examine life course findings in selected disorder groups. Detailed discussions of these disorders are presented in later chapters. Our aim here is to use emerging findings to illustrate more general developmental issues, focusing in particular on patterns of childhood–adulthood continuity. To begin, we focus on homotypic continuities in four selected disorder groupings (antisocial behaviors, depression, anxiety and exemplar neurodevelopmental disorders), chosen to reflect differing patterns of disorder onset and course. Following this, we explore the more complex heterotypic continuities identified in so much longitudinal research.

Antisocial behavior

Antisocial behaviors and delinquency were among the first aspects of child behavior to attract attention from longitudinal researchers; as a result, a good deal is now known about their basic developmental profiles and course (see Chapter 65). Many indicators of antisocial behavior show highly distinctive age-related trends: physical aggression, for example, is at its peak very early in childhood (Tremblay, 2010), while delinquency rises sharply across the teens, declining gradually in the early adult years. In addition, longitudinal data consistently highlight the paradox that while most severely antisocial adults were antisocial children, only perhaps half of antisocial children go on to show marked antisocial behavior in adult life (Robins, 1966).

These findings point to heterogeneity in the antisocial population, and a number of approaches to subtyping have been proposed (Lahey & Waldman, 2012). Moffitt's (1993) developmental taxonomy highlights age at onset as the core distinguishing feature; other well-established markers of heterogeneity include comorbidity with ADHD, distinctions between physically aggressive and non-aggressive behaviors, and the presence of associated callous-unemotional (CU) traits (see Chapter 68). Considered individually, each of these features predicts long-term continuities in antisocial behavior; investigators are still working to clarify whether they constitute different facets of a single high-risk sub group or separable associated risks.

A further striking feature of longitudinal findings in the antisocial field is the wide spectrum of adverse outcomes faced by young people with disruptive behavior problems later in their lives. Fergusson *et al.* (2004), for example, found that (in addition to continuities in antisocial behavior), childhood conduct problems were associated with poor educational and occupational achievements; problems in sexual and partner relationships; early parenthood; and elevated rates of substance use, mood and anxiety disorders, and suicidal acts. Subsequent studies have documented associations with poor health-related behaviors and markers of chronic disease early in adulthood (Odgers *et al.*, 2008) and later—in representative as well as high risk samples—with increased risk of premature death (Maughan *et al.*, 2014).

What accounts for this broad spectrum of adverse outcomes? First, genetic liabilities are almost certain to play some part. Longitudinal twin studies point to genetic continuity in general antisocial phenotypes from late childhood to early adulthood, along with new genetic (and environmental) influences in adolescence (Wichers *et al.*, 2013). In addition, early onset conduct problems, physical aggression, and CU traits—all of which carry high risks of persistence—are all strongly heritable. At the same time, child conduct problems are also strongly associated with adverse environmental conditions. Studies of gene–environment interplay highlight the complex ways in which genetic and environmental factors combine to impact risk for the persistence of disorder over time. On the one hand, genetic factors may *moderate susceptibility* to individual and family-based risks (see Chapter 24). In the Christchurch longitudinal study, for example, variations in the *MAOA* genotype interacted with factors as varied as maternal smoking in pregnancy, material deprivation, maltreatment, and lack of school-leaving qualifications to influence risk for adolescent and early adult offending (Fergusson *et al.*, 2012).

On the other, genetically influenced traits may affect *exposure* to adverse environments. It has long been known, for example, that aspects of children's temperament and behavior can evoke negative reinforcing responses from parents. Evidence is now emerging that similar processes occur with peers: as early as the kindergarten years, genetically-influenced hyperactive and disruptive behaviors can evoke peer victimization and rejection (Boivin *et al.*, 2013), while later in development, genetic factors contribute to affiliations with deviant peers (Kendler *et al.*, 2007). Across development, cumulating consequences of this kind can function to stabilize maladaptive behaviors, selecting antisocial young people into risk-prone environments, and restricting their opportunities for involvement in more positive relationships and roles.

For children with early onset conduct problems, developmental "cascades" of this kind seem likely to contribute in important ways to the persistence of antisocial behavior over time. Where adolescent onset problems persist, substance abuse has been highlighted as one especially salient "snare" that can hinder desistance from offending (Hussong *et al.*, 2004). In addition, antisocial young people may vary in the extent to which they have access to, or can benefit from, later positive experiences. Sweeten *et al.* (2013), for example, identified changes in antisocial peer affiliations and peer influence as among the strongest correlates of reductions in offending among adjudicated offenders, while Laub and Sampson (2003) highlighted the role of adult "turning point" experiences, including social attachments to work, and supportive marital relationships, in promoting desistance from crime. The great majority of offenders eventually desist; these findings point to intervention targets that may accelerate that process and help to break—or at least interrupt—chains of risk.

Depression

Developmental findings have also been salient in relation to depressive disorders, markedly changing conceptualization of depression over time. Before the 1980s many viewed depression as a predominantly adult disorder: pre-pubertal children were thought too immature to experience depressive disorders, and adolescent low mood was assumed to reflect normative teenage mood swings. A wealth of evidence from clinical and epidemiological studies has changed these views. It is now clear that, though uncommon (1–2%), depressive disorders do occur in pre-pubertal children, and that depressive-like phenomena are also observed in some children as early as the preschool years (Angold & Egger, 2007).

Despite these early manifestations, adolescence is now recognized as a particularly important life stage in the development of depression. First, rates of depression increase markedly across the adolescent years, with median 12-month prevalence estimates equivalent to those for adults (4–5%), and a cumulative prevalence as high as 20% across the teens. New onsets of major depressive disorder continue across the life course, but for many sufferers the disorder begins in the adolescent years. Second, unlike childhood depression, adolescent depression shows strong continuity to adulthood; in referred young people, initial remission is followed by a recurrence in around 50–70% of patients within 5 years (Thapar *et al.*, 2012). And third, the female preponderance typical of adult depression becomes clearly established in the teens. The emergent sex difference seems more closely linked to pubertal stage than chronological age, pointing to the likely role of hormonal factors (Angold *et al.*, 1999); sex differences in adolescent brain development and in the cognitive processing of stressful experiences may also contribute to rising rates of depression in girls (Hyde *et al.*, 2008).

Depressive disorders in childhood, adolescence, and adulthood are typically defined by the same underlying features; despite this, it remains unclear whether depression at these different ages does indeed reflect a single homogenous disorder or common etiology. Childhood depression differs from adolescent and adult depression in a number of important ways: the prevalence is lower, there is no marked gender difference, and continuity with adult depression is low. There are also important etiological differences, with twin studies demonstrating consistently lower heritability for depression in children than in adolescents or adults. Distinctions between adolescent and adult depression are less clear. Studies comparing the psychosocial risk profiles of "juvenile"- and adult-onset depression suggest that early adversity, parental neglect, and problematic peer relationships are more strongly associated with early-onset depression (Jaffee *et al.*, 2002). Others have argued, however, that such findings reflect recency of risk exposure, and that developmentally-salient stressors are associated with depression at all stages of the life-course (Shanahan *et al.*, 2011). Treatment responses also show developmental variation, with tricyclic antidepressants effective in adult but not in child or adolescent depression (Hazell *et al.*, 2002). It remains unclear whether these differences in risk correlates and treatment response reflect maturation of relevant neurobiological systems, heterogeneity in the underlying nature of depression, or stage of illness factors.

Given the high rates of recurrence in depression, studies of the mechanisms underlying continuity across developmental periods are especially important. Heritable factors clearly play a part here, contributing to stability in depressive symptoms in both adolescence and adulthood (Lau & Eley, 2006). In addition, extensive evidence suggests that—as with antisocial behavior—genes act in concert with environmental influences to increase both *susceptibility* to psychosocial stressors (gene–environment interaction) and *exposure* to stressful environments (gene–environment correlation). Maladaptive coping styles such as rumination, depressogenic cognitive biases, and difficulties in interpersonal relationships are both predictors and outcomes of depression, forming further contributors to recurrence risk (Abramson *et al.*, 2002). And finally, vulnerability to relapse and illness severity appear to increase across the course of depressive illness, becoming increasingly autonomous from severe precipitants as the number of episodes increases (Kendler *et al.*, 2000). Often referred to as "kindling," processes of this

kind suggest that depression itself may increase sensitivity to stress, so that in time even relatively minor everyday stressors can trigger a recurrence (Post, 2010; but see also Monroe & Harkness, 2005).

As these findings suggest, developmental studies have provided important insights into influences on both onset and recurrence of depression. More evidence is now needed on factors that distinguish young people with more and less benign courses of early illness, to maximize the contribution of developmentally-sensitive findings for prevention and treatment.

Anxiety disorders

Different issues arise in relation to anxiety disorders, stemming in large part from the complexities of current nosology, where numerous different anxiety diagnoses are defined. Debate continues over the utility of this approach, and whether other distinctions—derived, for example, from neuroscience frameworks—could provide a more appropriate basis for classification (Pine, 2007). Developmental findings can contribute to these debates.

Beginning with age at onset, it is now clear that there is meaningful heterogeneity in onset patterns among anxiety diagnoses: some typically onset in childhood, some in early adolescence, and some in late adolescence/early adulthood. Separation anxiety and specific phobias have the earliest onset ages; in the German Early Developmental Stages of Psychopathology (EDSP) study, 50% of these disorders had begun by ages 5 and 8 years respectively, and almost all cases had emerged by age 12 (Beesdo-Baum & Knappe, 2012). Rates of social phobia and OCD (obsessive compulsive disorder) rose sharply in early adolescence, while agoraphobia, panic disorder, and GAD (generalized anxiety disorder) became more common later in adolescence and early adulthood. These later onset disorders lack the circumscribed fears seen in childhood onset disorders, possibly indexing a developmental shift in the expression of anxiety with age, and raising intriguing questions about the mechanisms involved.

Much less diagnostic specificity is evident in findings on developmental course. Retrospective studies point to the persistence of early anxiety disorders and suggest a relatively chronic or recurrent course (see e.g. Kessler *et al.*, 2012). Prospective findings paint a rather different picture; while they confirm above-chance levels of homotypic continuity, they also report quite low rates of stability in specific anxiety diagnoses and—especially in younger age groups—a tendency for anxiety symptoms to wax and wane over time (Bittner *et al.*, 2007; Beesdo-Baum & Knappe, 2012). Onset of a first ("pure") anxiety disorder is often followed by the development of other anxieties in adolescence/early adulthood; in its turn, this "load" of anxiety predicts other adverse outcomes including depression, substance use, and suicidality, along with psychosocial difficulties and poor health and relationship functioning (Copeland *et al.*, 2014).

Follow-back findings from the Dunedin study (Gregory *et al.*, 2007) are broadly consistent with this view, with little specificity in the childhood–adulthood linkages involved; specific phobias in adulthood had a significant history of juvenile phobias, but other adult anxiety disorders were likely to have been preceded by a range of anxiety diagnoses. Alone among DSM-IV adult anxiety diagnoses, PTSD stood out in having a history of behavioral as well as emotional difficulties earlier in development (Koenen, 2010); in conjunction with other individual and family factors, these early influences appeared to play a key role in shaping both exposure and responses to trauma later in life. Finally, we note that recent evidence is providing empirical support for one pattern of childhood–adult continuity of longstanding clinical interest: the possibility that separation anxiety in childhood may be a precursor to panic disorder later in life. Rates of separation anxiety fall sharply in the early teens, but a recent meta-analysis has identified a significant association with later panic (Kossowsky *et al.*, 2013), and longitudinal twin study findings have identified a common genetic diathesis between separation anxiety disorder and panic attacks (Roberson-Nay *et al.*, 2012).

Relatively little is known about the mechanisms that contribute to the persistence or recurrence of anxiety across development. Twin studies point to genetic influences on stability, but also highlight more "developmentally dynamic" patterns, with attenuation of the genetic effects on some late childhood anxiety phenotypes by early adulthood, along with the emergence of new genetic influences later in development (McGrath *et al.*, 2012). In a follow-up of social anxiety disorders from adolescence to early adulthood, Beesdo-Baum and colleagues (2012) identified earlier age at onset, severity of avoidance, impairment, and a high number of catastrophic cognitions as associated with persistence and diagnostic stability. Established risk factors for the onset of anxiety disorders, including both behavioral inhibition and a family history of social phobia or depression, also signaled a poorer prognosis.

Behavioral inhibition is a strong risk factor for the development of anxiety disorders, and social anxiety in particular (Clauss & Blackford, 2012; see Chapter 8). A variety of environmental factors have also been implicated, including maternal personality, aspects of the mother–child relationship, and an oversolicitous, intrusive, or controlling parenting style (Degnan *et al.*, 2010). Evidence is now emerging that parenting can moderate temperamental vulnerabilities, with risks for anxiety disorders especially marked when behavioral inhibition occurs in the context of parental over control. Biased attention-orienting to threat—a well-established concomitant of many anxiety disorders—also appears to modulate associations between inhibition and disorder (Shechner *et al.*, 2012). In addition, aspects of the peer context may moderate, maintain, and possibly exacerbate temperamental influences (Degnan *et al.*, 2010). Inhibited children tend to be less socially competent than their peers; as a result, they are more likely to be excluded from peer groups, and may be targets of bullying—both factors

known to increase risk of anxiety disorders. To date, interpersonal processes of this kind have primarily been documented in early and middle childhood. We must await further evidence to determine how far similar relational processes occur later in the life course, amplifying the effects of early temperamental characteristics and increasing vulnerability to the persistence of anxiety beyond the childhood years.

Neurodevelopmental disorders

We conclude with a brief overview of the rather different issues raised by current findings on outcomes in some of the earliest onset disorders of childhood: the neurodevelopmental disorders. As discussed in Chapter 3, and in the individual disorder chapters, extensive effort continues to be devoted to improving our understanding of the etiology of these complex difficulties. Evidence on later outcomes is much more sparse, but current findings leave little doubt that neurodevelopmental disorders are lifelong conditions. In general, some diminution in core symptoms seems typical with age, but alongside this it is also clear that broader functional impairments persist at least to adolescence, and often to adult life. We focus here on findings in just two areas—autism spectrum disorders (ASDs) and ADHD—to illustrate some of the issues that arise.

Beginning with autism, a recent review of follow-ups to early adulthood (Howlin & Moss, 2012) concluded that although the severity of symptoms tends to decrease with age, adult outcome is very mixed, including for individuals with normal IQ. One of the longest-term follow-ups to date (Howlin *et al.*, 2013) found some improvements in core symptoms and language skills by middle adulthood, but psychosocial outcomes were often poor, and in some instances appeared to have deteriorated over time. Over half in this sample had never worked, or were long-term unemployed; the majority had little autonomy in terms of daily living; and most had no close friend. The samples studied to date were, of course, diagnosed some decades ago, before early interventions and specialist educational supports were generally available, and when only more severely affected children were likely to receive a diagnosis. Outcomes for young people with ASDs today may be more promising; current findings can still, however, provide important pointers to factors that underlie variations in long-term outcomes. Early difficulties in reciprocal social interaction appear to be important here (Howlin *et al.*, 2013), along with the extent and severity of core symptoms, the extent of cognitive impairment, and the presence of co-occurring psychopathology. Environmental supports may also be crucial; indeed, some reports suggest that lack of appropriate support in adulthood can have a more deleterious effect on outcomes than factors such as IQ. The transition to adulthood raises new and potentially difficult psychosocial challenges for many individuals with ASDs, yet appropriate support services in adulthood are often severely lacking. Recent years have seen major advances in the development of comprehensive diagnostic and intervention services for young children with autism; findings from long-term studies point to the need for equally effective interventions across the life span.

Evidence on adult outcomes of ADHD is more extensive, though again few studies have tracked samples beyond the early adult years. Most children with ADHD show persistence of symptoms in adolescence and adulthood, with inattentiveness slower to decline with age than hyperactivity/impulsivity. A meta-analysis of follow-up findings (Faraone *et al.*, 2006) showed that although only around 15% met full criteria for disorder in early adulthood, a further 50% continued to face impairments associated with residual symptoms. In addition, follow-up studies highlight a strong persistence of earlier conduct problems in children with ADHD, as well as new onsets of antisocial behavior and substance misuse in adolescence (Langley *et al.*, 2010a); heightened risks for health risk behaviors in adulthood (Olazagasti *et al.*, 2013); and a range of negative educational, occupational, and psychosocial outcomes that appear to persist at least to mid life (Klein *et al.*, 2012). Even when ADHD is diagnosed and treated, only a minority of individuals subsequently exhibit full functional and symptomatic recovery.

The persistence of symptoms and later impairments seems especially marked in those with co-occurring conduct disorder/antisocial behavior; in addition, initial severity, IQ, and poor childhood school and social functioning have also been found to predict persistence, as have parental psychopathology and family conflict (Cherkasova *et al.*, 2013). Despite continuing needs, clinical recognition and service provision in adulthood remains limited, and individuals with ADHD are often reported to become disengaged from services and treatment. Increasing awareness of the lifelong consequences of ADHD, improved transitions from child to adult mental health services, and continued support in adulthood are all increasingly underlined as important priorities (Young *et al.*, 2011).

As these brief overviews suggest, evidence from differing neuro-developmental disorders highlights that adult outcomes for affected individuals are often poor. The stability of core symptoms varies, and may indeed show some improvements with age; alongside this, however, effects on psychosocial functioning may be more marked in face of the more complex demands of adolescence and adult life. Current evidence points to the benefits of supportive social contexts in adulthood, and the crucial need for continuing, appropriate services for many individuals with neurodevelopmental conditions.

Heterotypic transitions and psychopathological progressions

In addition to these "homotypic" continuities, developmental studies also make clear that more complex, "heterotypic" transitions among apparently distinct disorders are far from uncommon. Because multiple disorders often co-occur, some of these observed associations may be "epiphenomenal"—the product (at least statistically) of associations among other disorders. As a result, the strongest basis for identifying

"independent" heterotypic transitions among disorders comes from prospective, population-based studies that assess multiple disorders over time.

Copeland *et al.* (2013a) have recently reported findings of this kind, bringing together data from three major long-term studies to examine diagnostic transitions in common disorders from childhood to adolescence, and from adolescence to early adult life. Overall, continuities across developmental periods were strong, and bivariate analyses highlighted numerous heterotypic as well as homotypic links. Once prior "comorbidities" were controlled, heterotypic linkages were less common, but still clearly emerged. Between childhood and adolescence, the most robust transitions were from ADHD to ODD (oppositional defiant disorder), and from both CD (conduct disorder) and depression to later substance use. Between adolescence and adulthood, depression, and anxiety cross-predicted; adolescent substance use predicted early adult depression; and both CD and ADHD were associated with increased risks of later substance disorders. Predictions from CD to internalizing disorders were not supported in adjusted analyses; predictions from adolescent ODD to early adult depression fell just short of significance. Copeland *et al.* (2013a) were not able to examine transitions within the years of childhood, or between more common disorders and either neurodevelopmental problems or schizophrenia. From other evidence, however, it seems likely that early transitions from ADHD to CD, associations between schizophrenia and earlier emotional/behavioral difficulties, and the emergence of emotional/behavioral difficulties in children with specific learning problems should be added to this list of "independent" heterotypic progressions.

How might patterns of this kind arise? Two broad types of explanation have been put forward: that heterotypic continuities reflect age-varying expressions of the same underlying liability, or that one disorder or its associated impairments constitute risk factors for a second, distinct condition. In practice, elements of both processes may often be involved and shared genetic vulnerabilities implicated. Behavior genetic analyses have consistently identified shared genetic influences on pairs of disorders; more recently, multivariate genetic studies have highlighted more widespread genetic pleiotropy, suggesting that most common forms of child psychopathology share some genetic liabilities (see e.g. Lahey *et al.*, 2011). It is also becoming clear that specific molecular genetic risk factors operate across different disorders (Owen *et al.*, 2011; see Chapter 24). From a developmental perspective, findings of this kind may suggest that the same genetically-based vulnerabilities are manifest in different ways at different stages in development, in part, perhaps, as a result of interactions with normative maturational processes or changes in young people's social worlds. Investigators are now beginning to identify heritable neurobehavioral vulnerabilities that may contribute to processes of this kind. In relation to progressions from childhood anxiety to adolescent depression, for example, changes in sensitivity to social evaluative threats around the time of puberty may constitute intermediate phenotypes of this kind (Silk *et al.*, 2012). Emerging evidence suggests that the brain systems involved in responding to social information may become more sensitive or active during puberty—a time when peer and romantic relationships are also growing in importance, and when social evaluations become increasingly salient. If confirmed, models of this kind not only move us closer to understanding how genetically-based vulnerabilities may contribute to transitions among disorders, but may also suggest new targets for intervention.

The value of examining pathways of this kind has also emerged in studies of progressions from ADHD to conduct problems. Here, replicated evidence has shown that the *COMT* val158met variant high-activity genotype is associated with increased risk for antisocial behavior specifically in the presence of ADHD (Caspi *et al.*, 2008). This gene variant has well-established associations with executive functioning, and also with problems in social cognition—both known correlates of antisocial behavior, and both thus plausible intermediate phenotypes. Langley *et al.* (2010b) tested both as potential mediators in the ALSPAC cohort; problems in social understanding were on the pathway from genotype to antisocial outcomes in children with ADHD, while measures of executive control were not. Once again, these findings may have clinical as well as theoretical significance, suggesting that interventions to improve social understanding in ADHD may reduce risks of the development of aggression and conduct problems.

Conduct problems figure prominently in reports of heterotypic continuity; indeed, follow-back analyses of early adult disorders in the Dunedin cohort showed that CD/ODD was part of the developmental history of *all* the young adult disorders assessed, including manic episodes and schizophreniform disorders (Kim-Cohen *et al.*, 2003). Progressions from CD to substance use are among the best-established associations, likely reflecting shared, genetically-based personality features. Here, however, associations are not simply unidirectional: CD predicts adolescent substance use, but early adolescent alcohol and cannabis use also predict subsequent delinquency. Mediating mechanisms appear to vary at different stages of substance use, with, for example, shared environmental influences most important for transitions to early alcohol use, but shared genetic liability the dominant influence on links between antisocial behavior and later alcohol dependence (Malone *et al.*, 2004). Once established, substance problems may affect persistence in antisocial behavior through a variety of pathways including neurobiological effects on disinhibition, peer influences, adverse effects on family relationships, and the need for money to support drink and drug habits.

In addition to progressions to other "behavioral" disorders, child and adolescent conduct problems have also frequently been associated with increased risk for depression. To date, progressions of this kind have largely been assumed to reflect "down stream" effects of conduct problems, whether via selection into stress-prone environments, the development of negative

self-cognitions, or, in some instances, the pharmacological effects of substance use. Recently, however, studies have begun to highlight the possibility of shared temperamental influences centering on irritability. Longitudinal findings suggest that ODD, rather than CD, may be the more salient predictor of depression risk (Copeland *et al.*, 2009), with irritable mood a key element in this progression; adolescent irritability has also been found to predict suicidality later in adulthood (Pickles *et al.*, 2010), and twin studies point to common genetic underpinnings with low mood (Stringaris *et al.*, 2012; see Chapter 5).

As these examples suggest, many developmental associations among apparently distinct disorders may in part at least reflect expressions of the same underlying liability. Some, however, do seem likely to reflect *psychopathological progressions*, whereby the experience of one disorder contributes, directly or indirectly, to risk for another. Though evidence is still limited, some emotional/behavioral concomitants of specific learning difficulties may be of this kind; links between reading difficulties and anxiety, for example, show no clear evidence of shared genetic influence in the twin samples studied to date (e.g. Whitehouse *et al.*, 2009), suggesting that reading problems may constitute a direct risk for the development of anxiety in some children. Associations between substance use and later depression provide a second, quite different, example. Links between these disorders are strong, raising important questions over both the likely direction of effects and the causal processes involved. In the case of alcohol abuse disorders, a recent review and meta-analysis concluded that links with depression could not be attributed to confounders; that evidence was strongest for an effect of alcohol abuse on depression; and that potential mechanisms include neurophysiological and metabolic changes resulting from alcohol exposure (Boden & Fergusson, 2011).

Long-term effects of early experience

We conclude by examining a different aspect of childhood–adult "continuity": links between adverse experiences early in development and risk for psychopathology later in life. The shorter-term sequelae of childhood adversities are examined in detail in Chapter 26. We focus here on evidence for their persisting impact beyond the childhood years; on issues involved in interpreting evidence on such long-term links; and on some of the intervening mechanisms that are likely to be involved.

There is by now extensive, well-replicated evidence of associations between exposure to early adversity and risk for both psychiatric disorder and poor physical health later in life. Both chronic stress and severe acute experiences seem implicated, spanning exposures as varied as maltreatment and neglect, maladaptive family relationships, parental psychopathology, depriving institutional rearing, bullying victimization, and socio economic disadvantage (Odgers & Jaffee, 2013).

Retrospective evidence for associations with adult outcomes comes from large-scale epidemiological surveys such as the Adverse Childhood Experiences (ACE) study (Dube *et al.*, 2001), where information on adult disease is linked to respondents' recollections of childhood. Studies of this kind have shown strong links between childhood adversity and adverse health sequelae across the adult years (Odgers & Jaffee, 2013). Long-term prospective follow-ups of both high-risk and epidemiological samples are now confirming these findings in an increasing range of areas. Prospectively-reported childhood family adversities, extra familial adversities such as bullying, and follow-ups of abused and neglected children all show substantial predictive associations with psychiatric disorder in adult life (e.g. Copeland *et al.*, 2013b; Horwitz *et al.*, 2001).

The consistency of these findings is compelling; nonetheless, some caution is required in interpreting their meaning. Statistical associations do not, of course, necessarily imply causation. Shared genetic liabilities may contribute to children's vulnerability to adverse experiences, but also to their exposure to them; as a result, associations between psychopathology and adversity may reflect reverse causation, or reciprocal influences that play out in complex ways over time (Sameroff & Mackenzie, 2003).

As discussed in Chapter 12, increasingly sophisticated analytic methods are now being applied to tease these differing possibilities apart. In some instances, evidence for causal influences has proved limited, once shared genetic and environmental confounders are taken into account. In others, correlated adversities may form elements in a causal chain, with, for example, the effects of distal risk factors such as poverty or parental divorce mediated via more proximal aspects of family functioning (Conger *et al.*, 1994). Early adversities rarely occur in isolation, and the clustering of adversities makes it difficult to identify unique risk effects. Traditionally, identifying specific influences has relied on multivariate statistical techniques, but these have inherent limitations; where possible, evidence from intervention studies, genetically sensitive designs and other quasi-experimental approaches provides for more powerful tests (see Chapter 12). Such approaches already provide evidence of the likely causal effects of a range of adversities on psychopathology in childhood; though currently more limited, genetically sensitive studies are also beginning to point to long-term causal influences (see e.g. Kendler & Gardner, 2001).

Studies are also clarifying other aspects of adversity-outcome associations. First, contrary to some early assumptions, most early adversities appear to show relatively nonspecific predictions to a broad range of later psychopathology (Gershon *et al.*, 2013), as well as impacts on cognitive development, educational, and occupational functioning, social relationships, and health (Odgers & Jaffee, 2013). Second, the effects of exposure to multiple adversities are cumulative. Childhood adversities often cluster, and negative adult outcomes are most common in those who experience multiple risks. In the ACE study, for example, the risk of suicide attempt was elevated 2–5 fold when individual childhood adversities were examined separately, but increased

up to 30-fold when the cumulative burden of adverse early experience was taken into account (Dube *et al.*, 2001).

Third, in relation to timing, it has been proposed that exposure to stress at critical periods of brain development may carry especially high risk for later psychopathology (Heim & Binder, 2012). In observational studies, however, it is difficult to identify discrete sensitive periods because so many risk exposures are chronic or recurring. At present there is little support for the notion that the risk effects of adversity are *confined* to particular sensitive periods, though there is evidence for developmental variation in risk effects. Studies of Romanian children adopted from extremely depriving institutions, for example, highlight not only that very early privation can have persistent deleterious effects on development, but also that age at placement is an important determinant of the degree of later impairment and post adoption catch-up (Rutter *et al.*, 2012).

Progress has also been made in identifying the range of mechanisms that may underlie the long-term effects of early adversity. Evidence on the biological embedding of early experience—how early adversity "gets under the skin"—is reviewed in detail in Chapter 23. Negative impacts may also be mediated via effects on cognitive, affective, and psychological development. Exposure to maltreatment, for example, has been shown to influence children's emerging capacity to regulate emotions; to contribute to deficits and biases in processing affective stimuli; and to lead to problems in social information processing (Dodge, 2006). In addition, problems in close friendships and intimate relationships are also common, depriving individuals of the benefits of supportive relationships, and studies of adult victims of maltreatment highlight increased exposure to further adverse life events (including revictimization) in adult life.

In part, long term risk effects may also be mediated by effects on early-onset psychopathology, though current evidence suggests that this is unlikely to provide a complete explanation. Data from the Great Smoky Mountains Study, for example, demonstrate that victims of bullying experienced elevated rates of psychiatric disorder in childhood, adolescence, and adulthood; when earlier psychopathology was accounted for, however, associations with adult psychiatric disorder remained (Copeland *et al.*, 2013b).

Finally, a universal finding is that there is substantial heterogeneity in long-term outcome following all kinds of early adversity (Rutter, 2013). Despite exposure to enduring and severe early stressors, many children maintain adaptive trajectories and achieve positive outcomes later in life. Understanding resilience of this kind is important for two reasons: it can cast new light on developmental processes and may also point to additional foci for preventative interventions— "risk buffers"—that can be promoted to mitigate the impact of early trauma and adversity when amelioration or removal of risk is not feasible.

Resilience is an interactive concept, involving the better-than-expected outcomes achieved by some individuals in the face of early adversity (Rutter, 2012; 2013). The processes that explain resilience (see Chapter 27) are likely to be fluid, encompassing varying psychological, social, and biological features at different stages in development. First, evidence of gene-environment interactions highlights that genetic factors play a role in moderating individual responses to stress. Second, psychological and cognitive processes are important; children differ in their perceptions and understanding of stressful and traumatic events, and those who do not attribute blame to themselves when parents separate, or in the context of maltreatment, are more likely to avoid negative psychological sequelae (McGee *et al.*, 2001). In addition, individuals' personal agency, along with their capacity to self-regulate emotions and plan for the future, are consistently associated with mental health and psychosocial outcomes in high-risk groups. Third, resilience studies indicate that the maintenance of positive social relationships, both with family members and with peers, may be especially important in the context of early adversity (Collishaw *et al.*, 2007); and for some individuals, the transition to adulthood can provide opportunities for positive "turning point" experiences—such as marriage—that can disrupt previously maladaptive trajectories (Jaffee *et al.*, 2013). Fourth, there may be important context-specific predictors; for example, enhancing community support and reducing stigma are promising targets for intervention in communities affected by AIDS (Betancourt *et al.*, 2013; see Chapter 46). And finally, although evidence of "steeling" effects in humans is still preliminary (Rutter, 2012), in some circumstances exposure to mild forms of stress may prepare individuals for dealing with more difficult challenges later in life.

Conclusions

As these brief sketches illustrate, although complex, connections across the life course are meaningful and strong, and a life course perspective brings both scientific and practice-oriented insights that would remain hidden in more developmentally "demarcated" research. Over time, developmental studies have contributed to our etiological understanding, highlighted the heterogeneity in pathways (both adaptive and maladaptive) that follow from childhood disorder, and underscored the possibilities for resilience, recovery, and positive turning points that arise throughout development. Though some long-term studies were initiated many years ago, most are of much more recent origin. This "first generation" of longitudinal research has already provided rich rewards, transforming thinking in numerous domains; we can expect equally rich—and equally challenging—insights as results from the next generation of studies begin to emerge.

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