Annotation: Psychopathology in Children with Intellectual Disability

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Recent advances are reviewed in understanding the heightened prevalence of psychopathology and maladaptive behavior among children with intellectual disability. Researchers have traditionally emphasized measurement and prevalence issues, using either psychiatric assessments or rating scales to identify the prevalence of various problems in children with intellectual disability. Yet the time is ripe to shift directions, and identify more precisely why children are at increased risk for psychopathology to begin with. Although several “bio-psycho-social” hypotheses are reviewed, a particularly promising line of work links psychopathology to genetic intellectual disability syndromes. Psychiatric vulnerabilities in several syndromes are reviewed, as are the advantages of phenotypic work for understanding psychopathology among children with intellectual disability more generally.

Keywords: Behavioral phenotypes, Down syndrome, dual diagnosis, fragile X syndrome, intellectual disability, Prader-Willi syndrome, Williams syndrome.

Abbreviations: ABC: Aberrant Behavior Checklist; ADHD: attention deficit hyperactivity disorder; DBC: Developmental Behaviour Checklist; PDD: pervasive developmental disorders; UPD: uniparental disomy.

Relative to their counterparts without delay, children and adolescents with intellectual disability are at increased risk for psychopathology (e.g., Gostason, 1985; Koller, Richardson, Katz, & McLaren, 1982; Rutter, Tizard, Yule, Graham, & Whitmore, 1976; see Bregman, 1991, for a review). These children show a wide spectrum of problems, including severe psychiatric diseases such as mood disorders and psychosis; disruptive behavior disorders such as attention deficit hyperactivity disorder (ADHD); maladaptive traits such as high anxiety or impulsivity; and a host of more specific features, such as stereotypies or self-injurious behavior. Further, as many as 30% of the individuals with intellectual disability may have autism or pervasive developmental disorders (PDD) (see Bryson, 1997, for a review).

Work over the last decades has focused primarily on measuring these problems, and identifying their prevalence in various samples of children with disabilities. Indeed, measurement and prevalence studies have formed the foundation of a fast-growing research specialty on mental illness in children with intellectual disability. This review thus begins with a brief overview of prevalence studies, focusing primarily on the multiple challenges in conducting this line of work.

With this prevalence foundation in place, the time has now come for researchers to build in other directions. In particular, we still do not know why children with intellectual disability are at increased risk for psychopathology to begin with. Etiological hypotheses cover the “bio-psycho-social” spectrum, from genetic etiology and neurological deficits to personality styles to social stigma. Of these hypotheses, genetic status holds particular promise, and the review highlights this line of work.

How Many Children with Intellectual Disability Have Psychopathology?

Prevalence Issues

Though a seemingly straightforward question, the prevalence issue is complicated by how psychopathology is measured, as well as by who is being assessed. Using population-based, epidemiological samples, estimated prevalence rates of overall psychopathology in people with intellectual disability fluctuate widely, from a low of 10% (Borthwick-Duffy, 1994), to 30–40% (Einfeld & Tonge, 1996; Reiss, 1990; Rutter et al., 1976), to a high of 70% (Gostason, 1985).

Even when examining specific diagnoses, rates remain very disparate. Table 1 exemplifies this variability, summarizing prevalence rates from population-based samples of mixed or nonspecific etiologies for three childhood disorders. Prevalence rates for hyperactivity/ADHD range from 7% to 21%; for autism/PDD from 2% to 41%, and for depression from 4% to 10%. Although not comprehensive, these figures aptly demonstrate the tremendous variability in prevalence rates across studies (for further review see Bregman, 1991).

Why is there such variability in prevalence rates? As summarized in Table 2, variable prevalence rates can be attributed to subject characteristics such as IQ, residential status, and etiology, as well as to measurement issues. Relative to those with mild intellectual disability, for

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1 Throughout the text this term is used as a synonym for “mental retardation” as defined by ICD-10/DSM-IV.
Table 1

Examples of Variable Prevalence Rates of Three Disorders in Children with Mixed or Nonspecific Etiologies

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Age</th>
<th>Method</th>
<th>Autism/PDD</th>
<th>ADHD</th>
<th>Depression/Anxiety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gath &amp; Gumley, 1986</td>
<td>154</td>
<td>6–17</td>
<td>ICD-9</td>
<td>2–16%</td>
<td>7%</td>
<td>10%</td>
</tr>
<tr>
<td>Gillberg et al., 1986</td>
<td>149</td>
<td>13–17</td>
<td>DSM-III</td>
<td>4–41%</td>
<td>11%</td>
<td>4%</td>
</tr>
<tr>
<td>Jacobson, 1982</td>
<td>8728</td>
<td>0–21</td>
<td>Behaviors</td>
<td>9–13%a</td>
<td>9–21%</td>
<td>0.3–4%</td>
</tr>
</tbody>
</table>

a Lack of interpersonal responsiveness.

Table 2

Sources of Variability in Prevalence Studies

- IQ level
- Different types of samples
- Epidemiological, outpatient, inpatient, residential center
- Mixed etiologic groups
- Different measures of psychopathology
  - Psychiatric illness: record-reviews of previous diagnoses in hospital, clinic or school files; DSM- or ICD-based interviews with parent and/or child as informant
  - Maladaptive behaviors: parent checklists and rating scales; teacher checklists, self-rating scales
- Differences in diagnostic nosologies over the years (DSM, ICD, idiosyncratic systems)
- Different criteria for “caseness”
  - Above threshold or cut-point on scales or checklists; psychiatric diagnoses; institutional ratings of symptom severity

Example, individuals at the lower end of the IQ spectrum are more likely to be diagnosed with behavioral disorders, including self-injury, aggression, autistic behaviors, and stereotypies (Borthwick-Duffy, 1994; Einfeld & Tonge, 1996; Jacobson, 1982). Many of these children are served in more intensive or specialized educational or residential programs, and rates of these behaviors are often highest in these settings (Rojahn, 1994).

Conversely, those with mild levels of delay are more likely to have conventional psychiatric diagnoses of anxiety, mood, or disruptive behavior disorders (Einfeld, 1992; Matson, Barrett, & Helsel, 1988). Indeed, among mildly retarded children referred for outpatient treatment, rates of conduct disorder are as high as 45%, and those of depression as high as 22% (Reid, 1980). Although these problems may be more common in those with mild levels of delay, it is unclear to what extent prevalence disparities are a by-product of the difficulties in making psychiatric diagnoses in low-functioning, less verbal individuals.

Variable prevalence rates of psychopathology are also associated with the predominant use of mixed etiology groups. Indeed, the vast majority of studies on psychopathology in children or adults with intellectual disability examine groups of subjects with heterogeneous causes for their delay (Dykens, 1995, 1996; Hodapp & Dykens, 1994). Although we return to this theme later, more consistent behavioral vulnerabilities are found when researchers examine discrete etiological groups.

Issues of Psychiatric Diagnoses

Discrepant ways of conceptualizing and measuring psychopathology are also leading culprits in variable prevalence rates across studies, with some researchers using psychiatric diagnoses and others using rating scales of psychopathology. Those who use psychiatric diagnoses assume that children with intellectual disability suffer the same psychiatric disorders as their nonretarded counterparts (Szymanski et al., 1998). Children with intellectual disability may, however, manifest symptoms in altered, more simplistic, or “masked” ways (Sovner, 1986), including behavioral shifts from baseline states (Reiss, 1994). Szymanski and colleagues offer examples of how symptoms of depression and other disorders might be shown in those with intellectual disability. Using these types of guidelines, many researchers have made psychiatric diagnoses even in those with moderate to severe levels of delay (Bouras, Brooks, & Drummond, 1994). Even in studies using psychiatric diagnoses, researchers have used different methodologies. Some prevalence studies, for example, have culled a priori diagnoses from medical records in clinics or hospitals, resulting in elevated rates relative to nonreferred samples. Other record review studies have sampled all clients receiving services from state departments of mental retardation (e.g., Borthwick-Duffy, 1994; Bruininks, Olson, Larson, & Lakin, 1994; Jacobson, 1990). Despite the advantage of large sample sizes, these departments often use idiosyncratic diagnostic categories that differ from state to state, which often limits generalizability of findings.

Improving on record reviews, some researchers make DSM or ICD diagnoses based on direct interviews of children with intellectual disability or their parents (e.g., Bouras et al., 1994; Moss, Prosser, Ibottoson, & Goldberg, 1996). It bodes well for future prevalence studies that the most recent versions of these systems, the DSM-IV and ICD-10, are more alike than different (Volkmar & Shwab-Stone, 1996). Even so, periodic changes in these nosological systems have made it difficult to compare prevalence rates for the same disorder over time. Further, inter-rater agreement may be inadequate when clinicians make DSM-IV or ICD-10 diagnoses in children with intellectual disability. Although such findings highlight the need for clinicians to receive specialized training in intellectual disability, they also suggest that traditional psychiatric diagnoses may not reflect the diversity of problems shown by these children.

Issues with Checklists and Rating Scales

Conversely, many researchers forgo categorical diagnoses altogether, and instead measure psychopathology with checklists or rating scales. These tools are particularly sensitive to the unusual behaviors shown by children with intellectual disability, such as stereotypies or self-injury (see Aman, 1991, for a review). Many rating scales have now been developed, yet the proliferation of these instruments seems a mixed blessing. On one hand, researchers and clinicians need psychometrically sound measures of psychopathology. Examples of particularly promising and commonly used scales “normed” on...
psychopathology in children with intellectual disability. Diagnostic accuracy improves when both patients and informants of their offspring's anxiety or depression. Diagnostic symptoms associated with anxiety or depression, as well as adults were more apt to report certain autonomic paring adults with intellectual disability to their parents, thereby reducing variability in prevalence studies. Com- much promise for improving diagnostic precision, or children themselves. Multi-method approaches hold views with the child and his parents, as well as through researchers adopt a multi-method, multi-informant ap- paring assessments of different behaviors, with different domains being fragmented or inconsistent, as they are based on tools are not always used for their intended purposes. Prevalence data across these various measures thus risk being fragmented or inconsistent, as they are based on assessments of different behaviors, with different domains and cutoff points for clinical significance.

In light of these concerns, some clinicians and researchers adopt a multi-method, multi-informant ap- proach. These diagnosticians assume that maladaptive behavior is best understood through psychiatric interviews with the child and his parents, as well as through behavioral rating scales administered to parents, teachers, or children themselves. Multi-method approaches hold much promise for improving diagnostic precision, thereby reducing variability in prevalence studies. Compar- ing adults with intellectual disability to their parents, for example, Moss and colleagues (1996) found that adults were more apt to report certain autonomic symptoms associated with anxiety or depression, as well as psychotic symptoms. Their parents, however, were more likely to report affective states and other symptoms of their offspring's anxiety or depression. Diagnostic accuracy improves when both patients and informants are interviewed, a lesson that seems equally relevant to children.

Table 3

<table>
<thead>
<tr>
<th>Domain</th>
<th>Sample Items</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reiss Screen (ages 12 and up)</td>
<td>Aggressive: tantrums, hostile</td>
</tr>
<tr>
<td></td>
<td>Autism: echolalia, withdrawn</td>
</tr>
<tr>
<td></td>
<td>Psychosis: delusions, hallucinations</td>
</tr>
<tr>
<td></td>
<td>Paranoia: overly sensitive, hostile</td>
</tr>
<tr>
<td></td>
<td>Depression-physical: eating problems, low energy</td>
</tr>
<tr>
<td></td>
<td>Depression-behavioral: sadness, anxious</td>
</tr>
<tr>
<td></td>
<td>Dependent personality disorder: anxious, attention-seeking</td>
</tr>
<tr>
<td>Developmental Behaviour Checklist (ages 4 and up)</td>
<td>Disruptive: impulsive, tantrums</td>
</tr>
<tr>
<td></td>
<td>Self-absorbed: overactive, flicks, taps, or twirls objects</td>
</tr>
<tr>
<td></td>
<td>Communication disturbance: echolalia, delusions</td>
</tr>
<tr>
<td></td>
<td>Anxiety: fears certain things, irritable</td>
</tr>
<tr>
<td></td>
<td>Autistic relating: resists being cuddled, doesn’t show affection</td>
</tr>
<tr>
<td></td>
<td>Antisocial: lies, steals</td>
</tr>
<tr>
<td>Aberrant Behavior Checklist (ages 6 and up)</td>
<td>Irritability, agitation, crying: hurts self, tantrums</td>
</tr>
<tr>
<td></td>
<td>Lethargy, social withdrawal: listless, isolated</td>
</tr>
<tr>
<td></td>
<td>Stereotypic behavior: repetitive movements, body rocking</td>
</tr>
<tr>
<td></td>
<td>Hyperactivity, noncompliance: impulsive, excessively active</td>
</tr>
<tr>
<td></td>
<td>Inappropriate speech: talks excessively, talks to self</td>
</tr>
</tbody>
</table>

Persons with intellectual disability include the Develop- mental Behaviour Checklist (DBC; Einfeld & Tonge, 1992), Reiss Scales (Reiss, 1988) and the Aberrant Behavior Checklist (ABC; Aman & Singh, 1994).

Yet each of these scales assesses distinctive sets of be- haviors, and each features different psychometric factor or domain scores. As shown in Table 3, for example, “anxiety” is a domain score on the DBC, an item on the depression and dependent personality domains on the Reiss, and not even measured on the ABC. Table 3 also shows how domain or factor scores differ across measures. Some diversity is expected, as the measures were developed for different reasons, but in reality these tools are not always used for their intended purposes. Prevalence data across these various measures thus risk being fragmented or inconsistent, as they are based on assessments of different behaviors, with different domains and cutoff points for clinical significance.

In light of these concerns, some clinicians and researchers adopt a multi-method, multi-informant ap- proach. These diagnosticians assume that maladaptive behavior is best understood through psychiatric interviews with the child and his parents, as well as through behavioral rating scales administered to parents, teachers, or children themselves. Multi-method approaches hold much promise for improving diagnostic precision, thereby reducing variability in prevalence studies. Compar- ing adults with intellectual disability to their parents, for example, Moss and colleagues (1996) found that adults were more apt to report certain autonomic symptoms associated with anxiety or depression, as well as psychotic symptoms. Their parents, however, were more likely to report affective states and other symptoms of their offspring’s anxiety or depression. Diagnostic accuracy improves when both patients and informants are interviewed, a lesson that seems equally relevant to children.

Why Are Children with Intellectual Disability Prone to Psychopathology?

Genetic and environmental causes of psychopathology among children in general can be used as a springboard into studies of children with intellectual disability. But simply applying existing causal models to children with intellectual disability ignores the robust finding that these children are at heightened risk for psychopathology. A more complete answer, then, needs to take into account distinctive aspects of the experience of having intellectual disability.

What are some of the distinguishing features of intellectual disability? An obvious first response is a low IQ, typically less than 70. It makes intuitive sense that children with diminished cognition also have fewer problem-solving skills to cope with the demands of everyday life, which may, in turn, lead to distress, anxiety, or aberrant behavior. This answer, however, masks a more complicated etiological picture. Multiple factors probably mediate the expression of psychopathology in this group of children, including psychological, familial, and social issues, as well as biological vulnerabilities such as genetic status. Salient hypotheses in each of these domains are now reviewed.

Psychological Factors

Psychopathology in children with intellectual disability may be associated with certain aspects of self-image and personality. Unlike their typically developing counterparts, these children generally show more global and less differentiated self-concepts, as well as less idealized views of themselves (see Evans, 1998, for a review). These views may set the stage for more negative or unrealistic appraisals of the self over time, which may be exacerbated by repeated exposures to failure. Given their cognitive and adaptive delays, many theorists emphasize that failure experiences dominate the learning histories of children with intellectual disability (e.g., Zigler & Bennett-Gates, 1999). Failure then contributes to feelings of uncertainty and “learned helplessness,” which in turn have been linked to depression and other problems (Weisz, 1990). Although children with intellectual disability risk failure, it is unknown to what extent these risks are offset by today’s emphasis on positive behavioral supports and inclusive settings (e.g., Koegel, Koegel, & Dunlap, 1996).

Certain personality styles of children may also be tied to psychopathology (Dykens, 1999a). As described by Zigler and colleagues, these include: an out-directed orientation whereby children look to others (instead of themselves) for solutions to difficult problems; aberrant social styles such as being either too wary or too disinhibited with others; and low expectancy or en- joyment of success (Zigler & Bennett-Gates, 1999). Possible maladaptive sequelae of these personality styles include low self-esteem, a distrust of the self, sadness, depression, dependency, withdrawal, helplessness, and impulsivity (Dykens, 1999a).

Familial Factors

Family stress has long been implicated in the poor adjustment of children with intellectual disability, and early workers assumed that families with children with
disabilities were inherently stressed or pathological (Solnit & Stark, 1961). Although family stress is often higher among families of children with disabilities, findings are contradictory and more recent studies emphasize family support and positive outcomes (see Hodapp, 1995, for a review). Contemporary approaches assume that how families fare—either positively or negatively—is mediated by child factors such as the child’s age, etiology, and IQ level, as well as by family factors such as degree of familial support, parental coping styles, parental maladjustment, and how parents perceive their child (see Minnes, 1998, for a review). A handful of workers have also described the heightened risks and needs for support among parents who themselves have intellectual disability (Feldman, Leger, & Walton-Allen, 1997).

Examining certain child variables, child psychopathology emerges as the single best predictor of family stress in families of children with Prader-Willi syndrome, Smith-Magenis syndrome, and 5p- syndrome, more so than age or IQ (Hodapp, Dykens, & Masino, 1997; Hodapp, Fidler, & Smith, 1998; Hodapp, Wijma, & Masino, 1997). Although the causal direction is unclear, an intriguing hypothesis is that these children’s genetic predisposition to certain types of psychopathologies sets in motion a series of parental responses that may, in turn, ameliorate or worsen these problems. Others, however, find evidence for environmental triggers that may contribute to child psychopathology, with marital discord and parental psychiatric disorder predicting maladaptive behavior in children with Down syndrome (Gath, 1990). Both family and child characteristics are implicated, and studies are needed that tease apart the role that each plays in the development of psychopathology in children with various conditions.

**Social Factors**

Social problems within or outside the family may also impinge on psychopathology. Both children and adults with intellectual disability are at heightened risk for exploitation and for physical and sexual abuse (Ammerman, Hersen, Van Hasselt, Lubetsky, & Sieck, 1994). Although the prevalence of abuse among this vulnerable population is unknown, maltreatment may exacerbate behavioral and emotional disturbance. Further, some adults with mild intellectual disability experience social stigma, and several studies show the deleterious effects of stigma on living and job opportunities, self-esteem, depression, and adjustment (Edgerton & Gaston, 1991; Reiss & Benson, 1985). Many persons with intellectual disability also show compromised “social intelligence” (Greenspan & Granfield, 1992), or inappropriate readings or responses to social cues—these may also contribute to stigma from others and exacerbate feelings of loneliness or isolation.

Similarly, children with intellectual disability risk peer rejection and ostracism. Peer relations are mediated, in part, by the ability of these children to negotiate peer conflict, as well as by how “different” they are perceived to be by their typically developing peers (Freeman & Kasari, 1998; Leffert & Siperstein, 1996). Even when children with and without intellectual disability become friends, these dyads are atypical in their lack of shared play, decision-making, and laughter, and in their hierarchical division of roles (Siperstein, Leffert, & Wenz-Gross, 1997).

Children with certain etiologies may be particularly susceptible to peer difficulties. Due to both their obesity and behavioral problems, children with Prader-Willi syndrome (compared to others with intellectual disability) are more apt to be teased and disliked by peers (Dykens & Kasari, 1997). Despite their sociability, children with Williams syndrome also have difficulty making friends, in part due to their anxiety, social disinhibition, and indiscriminate relating to others (Dykens & Rosner, 1999). Maladaptive sequelae of peer problems need further study in children with or without these genetic diagnoses, especially the extent to which peer problems are a precursor or by-product of psychopathology.

**Biological Factors**

In addition to genetic risk factors for psychopathology found in the general population (Rutter, Silberg, O’Connor, & Simonoff, 1999), children with intellectual disability experience more distinctive biologic vulnerabilities. These include seizure disorders, self-injurious behaviors, sensory impairments, and specific etiologies such as fetal alcohol syndrome and genetic syndromes. Seizures, for example, increase with lowering IQs, and are seen in as many as 30% to 50% of persons with severe to profound intellectual disability (see Bird, 1997, for a review). Epilepsy has been associated with many psychiatric conditions in children with intellectual disability, especially psychosis (e.g., Gillberg, Persson, Gruftman, & Themner, 1986; Lund, 1985), and problems related to behavioral dyscontrol (Bird, 1997).

Self-injurious behaviors are seen in 4% to 16% of large, epidemiological samples of individuals with intellectual disability; rates are many times higher among those with severe to profound delays or those residing in institutions (Rojahn, 1994). Behavioral factors have long been implicated in self-injury, yet more recent theories emphasize the need to integrate behavioral triggers with abnormalities in the endogenous opioid and serotonin systems (King, 1993). Different patterns or types of self-injury may be associated with different syndromes, including Lesch-Nyan disease (e.g. extreme lip and finger-biting), fragile X syndrome (e.g., hand-biting), Prader-Willi syndrome (e.g., skin-picking), and Smith-Magenis syndrome (e.g., head banging, nail-pulling, inserting objects into body orifices). These disorders may provide insights into biochemical anomalies associated with self-injury, such as the abnormal purine metabolism and dopaminergic function in Lesch-Nyan disease (Nyan, 1994).

As many as 17% of children with intellectual disability are deaf, and intellectual disability is found in approximately 30% of children with visual impairments and 60% of those with cerebral palsy (see Hodapp, 1998, for a review). Deaf children are three times more likely to show psychiatric disturbance than their hearing counterparts, especially anxiety and conduct disorders (Hindley, 1997). Certain types of motor impairments such as spina bifida-hydrocephalus and cerebral palsy are associated with hyperactivity and inattention (Wills, 1993). Blindness seems associated with a range of concerns, from adjustment and personality disorders to autistic-like presentations, especially among those with retinopathy of prematurity (Warren, 1994). Children with both intellectual disability and multiple sensory handicaps are
Table 4
Summary of Maladaptive Vulnerabilities in Children with Certain Genetic Syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Maladaptive vulnerability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fragile X</td>
<td>Social anxiety, shyness, gaze aversion, perseverence, autism/PDD, inattention, hyperactivity, sadness or depression (primarily females).</td>
</tr>
<tr>
<td>Williams</td>
<td>Anxiety, fears, phobias, inattention, hyperactivity, social disinhibition, overly friendly, indiscriminate relating, sensitive, emphatic.</td>
</tr>
<tr>
<td>Prader-Willi</td>
<td>Hyperphagia, non-food obsessions and compulsions, skin-picking, temper tantrums, lability, perseverence, stubbornness, underactivity.</td>
</tr>
<tr>
<td>Smith-Magenis</td>
<td>Inattention, hyperactivity, aggression, attention-seeking, self-injury, stereotypies (often with mouth), sleep disturbance, self-hugging.</td>
</tr>
<tr>
<td>Down</td>
<td>Noncompliance, stubbornness, inattention, overactivity, argumentative, withdrawn (depression and dementia among adults).</td>
</tr>
<tr>
<td>5p-</td>
<td>Infantile high-pitched cat-like cry, hyperactivity, inattention, stereotypies, self-injury, social, interests in communicating.</td>
</tr>
</tbody>
</table>

particularly vulnerable to emotional and behavioral problems (Hodapp, 1998).

Specific behavioral and psychiatric problems are seen as well in children with fetal alcohol syndrome (FAS) or fetal alcohol affects (FAE), now thought to affect about 2 in 1000 children in the United States (see Streissguth, 1997, for a review). These children are particularly prone to memory and abstraction problems, attention deficits, hyperactivity, poor judgement, and impulsivity, and as adults they often show depressive features. The educational and mental health needs of this population are considerable; in a study of 415 children with FAS or FAE, a full 80% were receiving treatment for their behavioral or emotional dysfunction and virtually all were judged to be in need of these services (Streissguth, 1997).

Finally, a particularly promising line of recent work links psychopathology to specific genetic syndromes. Sparked by remarkable advances in molecular genetics, such work on behavioral phenotypes aims to link together genes, brain, and behavior, as well as to refine treatment and intervention (Dykens, 1995, 1999b; Dykens & Hodapp, 1997; O’Brien & Yule, 1995). Although many researchers examine groups of subjects with mixed or unknown etiologies (Hodapp & Dykens, 1994), the movement is gaining speed to study the behavioral phenotypes of people with genetic syndromes. Witness, for example, the popularity of the annual meetings of the Society for the Study of Behavioural Phenotypes, the increase in genetic themes at conferences such as the NICHD-sponsored Gatlinburg meetings, and the flurry of recent publications on behavior in fragile X, Williams, Prader-Willi, Smith-Magenis, Down, and 5p- (cri du chat) syndromes. In light of these many contributions, psychopathology in these syndromes is now briefly reviewed (see Table 4). This review is far from complete, as there are now over 750 known genetic causes of intellectual disability (Opitz, 1996). Indeed, genetic disorders may account for as many as 41% to 51% of persons with intellectual disability living in the community or in institutions (see Dykens, Hodapp, & Finucane, in press, for a review). Even so, behavioral data are scant on most of these disorders, and six syndromes are reviewed here that have growing databases or particularly intriguing phenotypes that demonstrate the advantages of this line of work (for a review of more syndromes see O’Brien & Yule, 1995).

Fragile X syndrome. The most common known inherited cause of developmental delay, fragile X syndrome is caused by an excessive repetition of three nucleotide sequences (CGG) that make up DNA (see Bailey & Nelson, 1995, for a review). In addition to distinctive cognitive profiles and trajectories (see Dykens, Hodapp, & Leckman, 1994, for a review), people with fragile X syndrome are prone to a host of problems in relating to others, as well as to difficulties regulating their attention, arousal, and activity levels. Although these vulnerabilities are similar in type across gender, males are generally more severely affected than females.

Historically, fully affected males were often described as autistic, and this observation was evaluated in over 55 studies conducted predominantly during the 1980s (see Dykens & Volkmar, 1997, for a review). It is now appreciated that males with fragile X show a spectrum of difficulties in relating to others, from the relatively few who have full-blown autism (from 15% to 25%; see McCabe, de la Cruz, & Clapp, 1999) to the majority, who demonstrate social anxiety, shyness, withdrawal, a slow-to-warm stance, and gaze aversion. Some of these males have PDD-not otherwise specified (NOS) or anxiety disorders, and many show stereotypies, impulsivity, and sensitivities to sensory input. Unlike those with autism, most fragile X males recognize facial expressions and emotions and less activity in others (e.g., Turk & Cornish, 1998). Attention deficits and hyperactivity are seen to the majority of clinic and nonreferred males (e.g., Baumgardner, Reiss, Freund, & Abrams, 1995). Many of these problems with activity and sensory stimuli may relate to anomalies in the posterior cerebellar vermis and caudate nucleus (Abrams & Reiss, 1995).

The clinical picture is more variable among females with fragile X syndrome. These girls and women generally show similar though less severe problems with social anxiety, shyness, gaze aversion, and inattention (Lachiewicz & Dawson, 1994; Sobesky, Porter, Pennington, & Hagerman, 1995). Withdrawal, sadness, and relative weaknesses in interpersonal social skills are also seen. Some women also show depressive features, even as compared to other mothers of children with disabilities (Thompson et al., 1994).

For both males and females, the degree of involvement depends on the extent to which the trinucleotide CGG repeat is methylated, and the amount of fragile X protein (FMR1P) produced (Tassone et al., 1999). Fully affected males with intellectual disability produce no FMR1P, while males with mosaicism or partially methylated full mutations produce some FMR1P and generally have higher IQs. The amount of FMR1P produced by females
varies according to the random inactivation of either their affected or normal X chromosome, as does their degree of cognitive and physical involvement (Tassone et al., 1999). Although much progress has been made linking cognition in fragile X syndrome to molecular genetic and protein status, genetic ties to psychopathology are less well understood.

Williams syndrome. Williams syndrome is caused by a microdeletion on one of the chromosome 7s (7q11.23) that includes the gene for elastin (Ewart et al., 1993). The Williams syndrome cognitive-linguistic profile has come under considerable scrutiny; relatively less work has focused on the social-emotional functioning of these individuals.

In striking contrast to individuals with fragile X syndrome, persons with Williams syndrome are often cast as charming, outgoing, friendly, and emphatic (Dykens & Rosner, 1999; Gosch & Pankau, 1997). Persons with Williams syndrome may be as socially oriented as others with intellectual disability, but more apt to draw attention to themselves, to relate indiscriminately to others, and to empathize with the pain as well as positive affect of others (Dykens & Rosner, 1999). Despite their sociability, however, many persons with Williams syndrome have fewer friends than their counterparts, and they also risk exploitation or abuse as a result of their social disinhibition (Davies, Howlin, & Udwin, 1997; Dykens & Rosner, 1999). Sociability thus needs to be appropriately channeled through social skills training and social support systems (Dykens & Hodapp, 1997).

Social disinhibition may relate to certain maladaptive features common to those with the syndrome: inattention, over-activity, ADHD, impulsivity, and anxiety (e.g., Dykens, 2000; Einfeld, Tonge, & Florio, 1997). Although these problems are high relative to others with delay, anxiety seems particularly distinctive. In a recent study of 97 children and adults with Williams syndrome, 50% to 60% showed generalized or anticipatory anxiety (Dykens, 1999a). Even more striking was that relative to others, the vast majority had elevated fears and phobic symptoms, with 95% having marked or persistent fears for 6 months or longer, and 84% avoiding their feared stimuli or enduring them with distress (cf. also Davies, Udwin, & Howlin, 1998). Whereas a few fears related to the syndrome’s characteristic hyperacusis, most did not, and fears and phobias were also equally apparent in males versus females, and in children versus adults. It is unclear how fears and phobias might relate to altered or deleted genes that flank the characteristic Williams syndrome elastin gene deletion on chromosome 7. Even so, Williams syndrome is emerging as a model disorder to better understand the genetic and environmental contributions to phobia in persons with or without this developmental disorder.

Prader-Willi syndrome. Prader-Willi syndrome is caused in most cases (70%) by a paternally derived deletion on chromosome 15 (15q11-q13); the majority of remaining cases are associated with maternal uniparental disomy (UPD), or when both chromosome 15s are derived from the mother (see Dykens & Cassidy, 1999, for a review). Although best known for its characteristic hyperphagia and food preoccupations, children and adults with Prader-Willi syndrome are vulnerable to a host of other behavioral and psychiatric problems. Relative to others with intellectual disability, children with Prader-Willi syndrome show more frequent or severe temper tantrums, impulsivity, stubbornness, under-
disturbance is a strong predictor of behavioral problems (Dykens and Smith, 1998). Although the causal direction of the sleep–behavior relationship is unclear, increased daytime nap length is associated with fewer maladaptive behaviors, especially externalizing difficulties (Dykens & Smith, 1998). Although several genes have been identified in the deleted region on chromosome 17 associated with Smith-Magenis syndrome (17p11.2), their phenotypic significance remains unknown.

Down syndrome. Relative to others, children with Down syndrome (trisomy 21) generally show fewer maladaptive behaviors or serious psychopathology (Dykens & Kasari, 1997; Meyers & Pueschel, 1991). In this way, Down syndrome exemplifies how behavioral phenotypes include both protective and risk factors for psychopathology. Although hypotheses vary, lower rates of problems may be associated with the syndrome’s stereotypic friendly, outgoing, and “Prince Charming” personality, the wide availability of parent support groups, and knowledge of this syndrome among the general public. New work suggests that the syndrome’s characteristic “babyface” cranio-facial appearance may also be a protective factor. Relative to others with intellectual disability, photographs of children with Down syndrome were more apt to meet standard “babyface” criteria and to be judged by others as having personality traits associated with babyfaced persons in general, including being more immature, warm, kind, naive, honest, cuddly, and compliant (Fidler & Hodapp, 1999).

Even so, children with Down syndrome are far from problem-free. Indeed, from 15% of children and 20% to 38% of adolescents show behavioral or psychiatric difficulties, including disruptive disorders such as ADHD and oppositionality, as well as anxiety disorders (Gath & Gumley, 1986; Meyers & Pueschel, 1991). Further, from 65% to 77% of a sample of 35 children with Down syndrome were described as stubborn, argumentative, disobedient, inattentive, and prone to withdrawal (Dykens & Kasari, 1997). Withdrawal and anxiety/depression may increase with advancing age across childhood and adolescence (Dykens & Kasari, 1997), and this relation may be a harbinger of the increased risk of depression among adults with Down syndrome (Collacott, Cooper, & McGrother, 1992). The association between adults with Down syndrome and Alzheimer’s disease has also been well established, with most adults 40 years or older showing neuropathological signs of dementia, and about 50% of those 50 years or older showing clinical manifestations of dementia (Zigman, Schupf, Zigman, & Silverman, 1993).

5p- (cri du chat) syndrome. Initially named cri du chat syndrome, children with this micro-deletion disorder (at 5p15) generally have a distinctive, cat-like cry in infancy, and are subsequently prone to behaviors commonly seen among children with severe levels of delay. These include stereotypes, self-injurious behavior, tantrums, and impulsivity (Cornish & Pigram, 1996; Dykens & Clarke, 1997), as well as hyperactivity, distractability, and inattention (Dykens & Clarke, 1997; Wilkins, Brown, & Wolf, 1980). These behaviors are elevated relative to others with delay, with hyperactivity and distractability seen in 75% to 85% of a large cohort of 146 children with 5p- syndrome (Dykens & Clarke, 1997).

In contrast to early observations linking 5p- syndrome to autism, children with 5p- generally appear social, well-related, and interested in communicating with others. Social withdrawal and disininterest in others may, however, be seen in children with translocations as opposed to deletions (Dykens & Clarke, 1997). Other recent advances suggest that the syndrome’s characteristic cat-like cry is localized to 5p15.3, with remaining clinical features associated with deletions at 5p15.2 (Gersh et al., 1995). Recent findings also show a lack of correlation between the size of the deletion and level of developmental delay (Marinescu, Johnson, Dykens, Hodapp, & Overhauser, 1999), as well as more variability in prognostic and developmental outcome than initially thought.

Summary. As summarized in Table 4, then, each of these six syndromes shows a propensity for some psycho-pathologies or maladaptive behaviors over others. These vulnerabilities reflect the idea that behavioral phenotypes are best viewed as an increased likelihood or probability that people with a given syndrome will show that syndrome’s characteristic behaviors relative to those without the syndrome (Dykens, 1995). This probabilistic definition opens the door to research on genetic and psychosocial reasons for individual differences within syndromes; for example, how behavioral variability in fragile X syndrome might be attributed to FMR1 protein status, family stress, or early intervention. Similarly, as the size of the deletion in 5p- syndrome does not appear related to severity of developmental outcome (Marinescu et al., 1999), studies are needed that identify how other genetic mechanisms interact with environmental interventions to create the 5p- behavioral phenotype. And in Prader-Willi syndrome and Angelman syndrome, work still needs to identify genetic, developmental, and other reasons for the behavioral differences in those with deletions versus UPD (Dykens et al., 1999; Smith et al., 1997).

In addition to within-syndrome variability, phenotypic research also assesses between-syndrome differences. As shown in the review, many behaviors are shared across syndromes, or show only partial specificity (Hodapp, 1997). Overactivity and inattention, for example, are seen in both fragile X and Williams syndromes. Other behaviors seem unique to a given syndrome, or show total specificity. Examples of total specificity might include hyperphagia in Prader-Willi syndrome, the cat-like cry in 5p- syndrome, and perhaps the self-hug in Smith-Magenis syndrome.

Between-syndrome, comparative studies pose certain methodological challenges, primarily in who should constitute the comparison or control group. Depending on the hypothesis of interest, comparison groups could be comprised of persons with intellectual disability of mixed etiologies, nonspecific delay, another syndrome group, or typically developing children matched on either mental age or chronological age (Hodapp & Dykens, 2000). Comparative studies are important in that they help differentiate shared from unique syndromic behaviors, and refine phenotypes in ways that may “fast-track” our understandings of gene function (Dykens, 1999b).

Taken together, within- and between-group studies are complementary approaches that help round out the phenotypic picture of individuals with genetic syndromes associated with intellectual disability. These approaches also refine the behavioral phenotypes of genetic disorders that do not involve intellectual disability, but instead show distinctive cognitive or linguistic profiles, such as velo-cardio-facial syndrome, Turner syndrome, or Klinefelter syndrome (see Dykens et al., in press, for a review).
Next Steps

Considerable work still needs to be done to complete our understanding of why children with intellectual disability are at heightened risk for psychopathology. As shown in this review, multiple psychological, familial, social, and biological factors are implicated, and many children with intellectual disability have compromised functioning in more than one area. In this vein, the term “dual diagnosis,” often used to describe persons with intellectual disability plus a psychiatric disorder, seems misleading and simplistic. Instead, many of these children have multiple problems, and multiple bio-psycho-social factors are likely to be involved in the etiology of these problems. Each causal factor may weigh differently for any given child, each may change in importance over the course of development, and many factors are also interdependent, one influencing the other over time.

Researchers can begin to capture these complexities through a variety of newly developed statistical and methodological advances. For example, few studies on psychopathology in intellectual disability have yet used individual growth curve analysis and latent variable modeling, which quantifies individual differences in growth and relates such variations to background variables (e.g., Methen & Khoo, 1998). These methods rely on the careful selection of predictor variables (e.g., age, IQ, gender, genetic diagnosis, family stress, SES, peer relations), and measurable outcomes (e.g., psychopathology, maladaptive behavior) taken at various points over time. To date, however, the relative importance of various predictor variables remains unknown for most types of psychopathology, making it uncertain which variables are the best candidates to enter into growth curve models.

As a first step, it may be easiest to examine the evolution of psychopathology in persons with known genetic syndromes associated with intellectual disability, as these studies would help disentangle certain genetic from psychosocial risk factors for psychopathology. This strategy assumes that even children with distinct genetic etiologies are subject to psychological, familial, social, and other background factors that shape their psychopathological outcome. Assuming that syndromic status would account for some but not all of the variance, subsequent work could then identify similarities and differences in how psychopathology evolves in children without known genetic syndromes.

Applying this line of thinking to Williams syndrome, for example, it may be that an outcome such as increased anxiety or phobia is mediated by both etiology-specific and shared factors (Dykens, 2000). Etiology-related factors could include a specific genetic vulnerability associated with chromosome 7, as well as hyperacousis, as some phobias in persons with Williams syndrome are related to sound (e.g., fears of sirens or thunderstorms). Hyperacousis may also set the stage for a startled, apprehensive response to other stimuli. Another frequent fear in Williams syndrome, falling from high places, may relate to the problems with gait, balance, and coordination shown by many persons with this disorder. Phobias in children with Williams syndrome may also be associated with risk factors seen among children in the general population, including nonspecific genetic factors, family history of anxiety, parental reinforcement of fear, environmental trauma, and a cognitive stance that overestimates fear (Craske, 1999).

Thus, whereas some of these causes are specific to Williams syndrome, others are shared and may also influence how phobias develop in intellectually disabled children without Williams syndrome. Similarly, ties between OCD and children with Prader-Willi syndrome may ultimately shed light on the etiology of these problems in other children with or without intellectual disability (Dykens et al., 1996). Findings from genetic syndromes, then, can help sort out the relative contribution of multiple genetic and other bio-psycho-social risk factors for specific types of psychopathology.

How psychopathology develops in children with intellectual disability may also depend on the interplay over time between risk and protective factors. On a much smaller scale, for example, family stress in Williams syndrome seems associated with both positive and negative aspects of the child’s personality. Aggressive or attentional problems in Williams syndrome children are predictors of family stress, yet such risks are buffered or offset by positive effects of these children’s social, empathic, kind-spirited personalities (Fidler, Most, Hodapp, & Dykens, 2000). Broadening this line of thinking, and borrowing from the extensive risk and resiliency literature, both risk and protective factors probably contribute to individual differences in psychopathology among children with intellectual disability.

In building a future research agenda, then, the time seems ripe for researchers to shift their emphases from earlier topics of prevalence and measurement to issues of etiology. Prevalence studies are still needed to inform the field about the scope of the problem, and measurement studies are needed accurately to tally and assess children with comorbid intellectual disability and psychopathology. Indeed, these two lines of work are inextricably linked, and recent advances in the psychiatric and psychometric assessments of children with intellectual disability should help reduce variability in prevalence studies. Yet these studies should not be accomplished at the expense of work that tackles the enduring questions of why children with intellectual disability are at risk for psychopathology, and why children differ in their proneness to these problems.

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