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Diagnosing Autism in Individuals with Known Genetic Syndromes: Clinical Considerations and Implications for Intervention

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Abstract

Assessing symptoms of autism in persons with known genetic syndromes associated with intellectual and/or developmental disability is a complex clinical endeavor. We suggest that a developmental approach to evaluation is essential to reliably teasing apart global impairments from autism-specific symptomology. In this chapter, we discuss our assumptions about autism spectrum disorders, the process of conducting a family-focused, comprehensive evaluation with behaviorally complex children and some implications for intervention in persons with co-occurring autism and known genetic syndromes.

Recent advances in genetics have led to increased recognition of many genetic syndromes underlying intellectual and developmental disorders (Abrahams & Geschwind, 2008; Jones, 2006). The field of behavioral phenotypes is also flourishing, as scientists and clinicians are identifying sets of characteristics that tend to be observed in persons with particular genetic syndromes. As others have stressed, it is important to consider that behavioral phenotypes are probabilistic in nature—having a particular syndrome does not predetermine one's personality structure, cognitive strengths or challenges; however, a particular genotype does impact the likelihood that certain characteristics will be observed in a given individual (Dykens, Hodapp, & Finucane, 2000). Genetic-environment interactions most certainly impact phenotypic presentation, and any scientific endeavor seeking to identify commonalities within behavioral phenotypes must highlight the importance of within-syndrome heterogeneity and the diverse presentation that will be observed, even in a carefully defined genetic syndrome (Dykens & Hodapp, 2001).

An interesting scientific and clinical challenge emerges with the consideration of behaviorally defined conditions within the context of a known genetic syndrome. For example, anxiety disorders are fairly common in persons with fragile X (FX) syndrome, but are not universal to all people with this complex neurodevelopmental condition (Einfeld, Tonge, & Turner, 1999). Knowing that a child has fragile X syndrome alerts practitioners and parents to the possibility of co-occurring anxiety, which can help caregivers to interpret a child's behaviors with greater sensitivity and more accurate attributions. Prevention and management efforts can also be directed toward the underlying issue (anxiety), either

through medical interventions, sensory-motor approaches or psychosocial strategies. Consider a child with fragile X syndrome who becomes agitated in a crowded place and impulsively runs out of the room without considering the possible consequences to his or her safety. If this behavior is interpreted as noncompliance (i.e., not following directions and remaining with an adult), then it is likely that the behavioral strategies employed to prevent the behavior and reduce its occurrence will be compliance based, focused on the behavioral endpoint that is relevant to the adults in the child's life, but not necessarily central to the underlying function of the escape-motivated behavior. If, however, the child's caregivers recognize the underlying anxiety, which has become manifest in a sort of fight-or-flight response, then they can focus their efforts on coaching the child to learn to cope with anxiety, perhaps using gradual desensitization approaches, teaching the child to self-monitor and self-regulate arousal, and to communicate his or her distress (Poindexter, 2000). Antianxiety medications could also be useful for reducing the physical discomfort of overwhelming somatic sensations (Levitas, 1996).

Similarly, understanding if a person with an intellectual or developmental disability also has an autism spectrum disorder (ASD) can provide important insights into prevention, management and intervention for the individual and for the family. As with anxiety disorders, autism is behaviorally defined and diagnosed, based upon observations and interviews that provide a comprehensive picture of the individual's developmental history and current functioning with regard to social reciprocity, nonverbal communication, and range of interests and activities. As with an anxiety disorder, there is no definitive medical test for autism, and the identification needs to be made by a person with expertise in both typical and atypical development.

If autism is part of the clinical picture, then there are implications for interpreting the child's behaviors and designing appropriate educational and therapeutic programs that address the core aspects of the autism behavioral phenotype—primarily difficulties in social relatedness and intentional, flexible communication and behavior. Teaching strategies, instructional settings, interaction styles, and expectations for progress may differ markedly if a child with a known genetic syndrome also presents with autism (Howlin, Wing, & Gould, 1995; Molloy et al., 2009).

Co-occurring autism has also been shown to impact parent stress and family adaptation in significant ways across the lifespan, particularly if it is identified later in childhood (Blacher, Kraemer, & Howell, 2010). Parents of children with a known genetic etiology for their intellectual impairment may feel confused by the differences they see in their own child, relative to others with the same genetic condition. For example, many parents of children with Down syndrome are likely to anticipate that their child will grow to be friendly, sociable, motivated by praise and invested in relationships with others. If a child with Down syndrome also has autism, then these social strengths are likely diminished, or at least, less consistent than in other children (Hickey & Patterson, 2006). Parents who have already been faced with the challenges of adjusting to raising a child with special needs may now find that they need to readjust to needs and challenges they did not anticipate. Families report feeling increasingly isolated if their child develops in a way that is not consistent with how his or her peers with the same genetic condition are developing (Hepburn, Philofsky, Fidler,

& Rogers, 2008). Communities of support built around specific diagnostic entities (e.g., Down syndrome, 22q deletion) may not feel as accessible or as encouraging when one's child is, in a sense, “twice exceptional.”

This chapter is focused on the process of conducting evaluations for autism in persons with a known genetic syndrome associated with intellectual and/or developmental impairments. There are several excellent reviews of the existing literature on the co-occurrence autism and genetic syndromes (Cohen et al., 2005; Lo-Castro, Benvenuto, Galasso, Porfirio, & Curatolo, 2010; Moss & Howlin, 2009; Nordin & Gillberg, 1996) and we will not focus on epidemiological aspects of comorbidity in this chapter. Rather, we will emphasize the process of determining whether or not autism is present and is a relevant additional diagnosis for an individual with a genetic syndrome. Beginning with a brief overview of our assumptions about autism, we will attempt to synthesize the existing research on the behavioral phenotype of autism within the context of specific syndromes. We will then explore some considerations for the evaluation process that are specific to working with a child with a known genetic syndrome. We will also share some clinical observations that influence our thinking about this topic. We will highlight when these observations are anecdotal and not empirically substantiated, in the hopes that others may consider some of these ideas worthy of further study.

1. Assumptions Concerning Autism Spectrum Disorders

The following assumptions underlie our approach to evaluating autism symptoms:

- Autism is behaviorally defined, and is characterized by qualitative impairments in social-communicative functioning in the presence of a limited set of interests and routinized behaviors. By “qualitative impairments” we echo Szatmari, Bartolucci, Bremmer, Bond, and Rich (1989), Wing (1976), and Rutter (1999) who emphasize a distinctive difference in the frequency, consistency, richness, integration, and fluidity of social and communication behaviors as characteristic of autism, relative to an individual's overall developmental functioning.
- The clinical presentation of autism varies across development. Symptoms that are relevant in toddlers are different from the symptoms that indicate autism in older children (Charman & Stone, 2006; Lord et al., 2006). If a child does not have a developmental delay, chronological age comparisons can be used to determine if the child's social-communication skills are more impaired than would be expected for his or her age. If the child has a developmental delay, mental age estimates should be used to evaluate the discrepancy between the child's social-communicative abilities and his or her overall developmental functioning (de Bildt et al., 2004; Lord & Richler, 2006).
- Autism is a disorder of brain development that is evident in the first 3 years of life (American Psychiatric Association, 2000; Charman & Stone, 2006; Courchesne, Redcay, Morgan, & Kennedy, 2005). There are different ways that brain development appears to be altered in the pathogenesis of autism, so the course and severity of symptom expression can differ markedly within individuals with this

diagnosis (Geschwind & Levitt, 2007). Thus, the field has adopted the notion of the "Autism Spectrum" in order to capture the diversity of the clinical presentation within the context of a triad of common impairments (e.g., social relatedness, nonverbal and verbal communication, restricted interests and behaviors) (Jones & Klin, 2009).

- Autism is strongly genetic. Multiple genes are thought to be involved, influencing a complex array of neurological, metabolic, neurochemical, and neuromodulating systems that lead to autism (Geschwind & Levitt, 2007; Skuse, 2007). Several estimates suggest that the heritability factor of autism is 0.90 or higher (Bailey et al., 1995; Spence, 2004). Genetic studies have identified some candidate loci on several different chromosomes (see Happe & Ronald, 2008, for review). Microdeletions and *de novo* copy variants also have been implicated in the epigenesis of autism (Abrahams & Geschwind, 2008; Minshew & Williams, 2007; Pinto et al., 2010; Zhao, Leotta, Kustanovich, Lajonchere, & Geschwind, 2007). Ghaziuddin (1997) suggested that family history of autism is an important risk factor to consider when conducting an evaluation for ASD in a child with a known genetic syndrome associated with developmental disabilities.
- Many individuals with autism also present with co-occurring medical, psychiatric, or functional disorders, including anxiety, depression, sleep disturbances, problems with daily living skills such as eating and toileting, motor impairments, difficulty regulating attention and affect, difficulty modulating responses to sensory inputs, coordinating and integrating perceptions and actions, language impairments, learning disabilities, and significant cognitive impairments (Coury, 2010).
- Social and communicative skills are diminished, but not entirely absent in persons with autism. Intellectual capacity, intervention experience, interpersonal supports and environmental modifications are thought to contribute to improved social and communicative functioning over time (Klin, Jones, Shultz, & Volkmar, 2005; Klinger, Dawson, & Renner, 2005; Landa, 2000).
- Intensive intervention is thought to be critical for promoting skill development for persons with autism (Rogers, 2000). Adaptive skills, such as toileting, are often learned through observation and imitation in typically developing children. However, for most young children with ASD, imitative learning is not the preferred instructional modality (Nadel, 2002). Rather, direct instruction is often required to teach new skills, and the process of communication may need to be taught before more advanced learning can take place (Prizant, Wetherby, & Rydell, 2000).
- Individuals may behave very differently in different situations and generalization of skills across people and/or settings is often difficult. "On-line" social processing is thought to be particularly impaired, and a person with autism may function markedly better in structured situations than in more spontaneous interactions (Klin et al., 2005).

2. Assessing Autism Symptoms in a Child with a Known Genetic Disorder

The following section of this chapter provides a clinical perspective on the process of determining if a child with a known genetic condition associated with intellectual disability may also have an ASD. There are a number of considerations when assessing a child with a known genetic disorder that make the evaluation process somewhat more complex. These issues are addressed individually.

2.1 Integrating clinical observations Into practice

The research base concerning the phenomenology of complex, co-occurring disorders of intellectual and/or developmental functioning is growing; however, more population-based studies are needed. Clinical impressions of those with known genetic disorders and ASD provide a rich, albeit complex, impression of how these phenotypes may vary within known genetic syndromes. Table 9.1 outlines some of these observations, along with clinical studies that describe these complex phenotypes. Although these data provide an integral starting point, future research will be needed to better understand how the autism phenotype varies within known genetic disorders.

Given the heterogeneity of symptom expression we might expect from such a complex phenotype, it is important for clinicians to develop an “inner database,” built through clinical experience with persons with complex behavioral phenotypes and their families. It is also important to remember the probabilistic nature of behavioral phenotypes (Dykens & Hodapp, 2001)—there is no “one way” two disorders will present when they co-occur, but there may be a tendency for certain behavioral characteristics to be more pronounced or qualitatively distinct in character than is observed in peers with one, but not both, conditions.

2.2 Conducting a comprehensive evaluation

Parameters for best practice in autism identification specify that a diagnostic evaluation should include a comprehensive evaluation of autism symptoms, incorporating both parent/caregiver report and direct clinical observations (see Filipek et al., 2000; Ozonoff, Goodlin-Jones, & Solomon, 2005). It can be helpful to observe the child's social and communication skill both within direct interactions with an unfamiliar clinician and also with familiar people in familiar situations. If possible, observing the person in spontaneous social interactions with peers can be very informative.

2.2.1. Interpret standard “cut points” with caution—If the person being assessed presents with significant cognitive impairments, it is particularly important to rely on the Best Estimate Clinical Diagnosis of an experienced clinician than to depend upon psychomet-rically generated cutoff scores (Risi et al., 2006). For example, research on the Autism Diagnostic Observation Schedule (ADOS, Lord, Rutter, DiLavore, & Risi, 1999) has led the developers to recommend caution when interpreting algorithm scores for persons with a mental age of less than 18 months (Lord et al., 1997).[1] Instability in algorithm scores when the mental age is this low makes inclusion of parent reports of behaviors and symptoms imperative.

2.2.2. Consider observed and reported symptoms within a developmental context—Assessing the child's developmental functioning is important for determining a "set point" for expectations of social and communication progress. The challenge of the evaluation is teasing apart a developmental delay from a developmental deviance that cannot be explained by the specific behavioral phenotype of the known genetic syndrome. In many situations, the individuals' overall developmental level—or overall cognitive potential—becomes the baseline from which to examine a person's adaptive skills (Howlin et al., 1995).

As part of the assessment of a child's adaptive behavior, it is particularly important to directly assess the child's social and communicative skills relative to his or her chronological and developmental ages. Given that ASD is often characterized by social and communication skills that are below expectations for chronological age and intellectual potential, the relative difference between an individuals' social and communicative functioning and his or her overall intellectual potential is critically important information. Developmentalists argue that only when one's social skills are below expectations for developmental age is autism potentially relevant (Lord & Richler, 2006). That is, if a child is functioning as would be expected for his or her developmental age, then autism is not, likely, a valid diagnosis.

For example, a 7-year-old child with an estimated developmental age of 2½ years would be expected to be imitating and initiating joint attention, but may not be engaging in reciprocal social play with peers or demonstrating much pretend play. Lack of peer relationships and imaginary play, therefore, would not be indicative of an ASD in this particular child because one would not expect this given the child's developmental age. On the other hand, deficits in shared affect, attention and attempts to engage through imitation would be seen as developmentally relevant signs of ASD for such a child.

In a contrasting example, consider a 9-year-old child whose overall developmental level is approximately 12–16 months. One would expect attention to faces, sharing affect, social orienting, and attempts to engage in simple social games with few motor demands. Functional play is not likely to be well developed, initiating joint attention may be harder to coordinate than responding to another's bid for attention, and imitation may just be emerging, especially if the child has significant motor impairment. Complexity of communication is likely to be limited, but intentionality and use of eye gaze or gesture could be expected as a means for indicating preferences, with our without coordination. If this particular child were to fail to orient to his or her name, not respond to social bids by familiar persons, lack affect sharing and engagement in simple social games, then it is possible that a co-occurring ASD is a valid conceptualization. In this example, the child's social and communicative engagement are not commensurate with his or developmental level, even when overall development is significantly compromised.

It is worth remembering that across most genetic syndromes that we can recall, most individuals with co-occurring autism are reported to make slower developmental progress,

[1]With the recent publication of new scoring algorithms for the ADOS, some of the measurement errors may be addressed within the tool; however, further study arc necessary to determine if the revisions contribute to improved specificity of the ADOS in discriminating co-occurring ASD.

relative to their peers with the same genetic condition, but without the autism (Baieli, Pavone, Meli, Fiumara, & Coleman, 2003; Bailey, Hatton, Skinner, & Mesibov, 2001; Baker, Piven, & Sato, 1998; DiGuiseppi et al., 2010). Slow progress could indicate a co-occurring condition (such as autism), or it could be associated with a particularly pervasive or severe form of the underlying genetic condition. Functional problems in sleeping, eating, or overall health can also impact the rate of developmental progress observed, and should be investigated (Batshaw, Pellogrino, & Roizen, 2007). Family stressors and significant life events can also adversely impact a child's receptivity to intervention (Guralnick & Cordon, 2007). The child's temperament may not be a good fit for the intervention approach, thus compromising adaptive gains (Hepburn, 2003). Therefore, a lack of developmental progress should signal further assessment, of the child, the interventions, and the social/educational context. Overall, if a child is not responding to quality interventions, it is important to consider shifting the intervention approach, regardless of whether or not there is a secondary condition to identify. As with other aspects of the behavioral phenotype of the specific syndrome, it may be helpful to know the relative developmental progress that can be expected for most persons with a particular syndrome. These are summarized in Table 9.2.

2.2.3. Examine motor functioning and consider its impact on social and communicative behaviors—Understanding a child's motor skills history and current profile is also an important consideration in the evaluation of autism symptoms in children with a known genetic disorder. If a child is not yet reaching for objects, not yet walking, not able to hold objects, control his or her eye gaze, track movements or alert to sound then one has to be particularly careful about attributing any difficulties using nonverbal behaviors as forms of communication as signs of autism. The problem is that absent nonverbal communication could be the result of either motor difficulty, or a lack of communicative intent. Moreover, if the individual's other skills are at a 3–6 month developmental level, then it is, in our opinion, not possible to conduct a valid evaluation for autism with our current tools and knowledge base. Only if the child could be reasonably assumed to have the motor skills necessary to engage in purposeful shared social smiling, differentiating a parent's voice, and orienting to others can we evaluate the social quality of these behaviors. These skills are usually noted by 8–10 months of age, which is probably the minimal age to consider ASD for any child, given the current research on symptoms in infancy (Ozonoff, 2009). In our experience, clinicians rarely feel comfortable offering more than a provisional identification of an ASD in children with known developmental motor delays under the age of two, and often recommend a re-evaluation in 1–2 years, after the child has had the benefit of early intervention and the opportunity to develop important core skills.

2.2.4. Review information on typical developmental trajectories—Many clinicians spend the majority of their time observing and working with children with atypical development, and it can be very helpful to refer to the developmental literature for summaries of timelines and expected milestones. See Table 9.3 for a summary of developmental milestones in social and communicative functioning.

2.2.5. Individualize the assessment battery—The determination of the relevant areas for further assessment may be influenced by the particular generic disorder presented by the

individual. Relying upon the research on the specificity of the comorbid ASD phenotype by syndrome, one may be able to develop an individualized assessment battery that targets skill areas that differentially expressed if the child also has ASD. For example, in a person with fragile X syndrome, one would expect to find a relative weakness in both receptive language and imitation skills in persons with FX and autism, relative to those without an ASD (Philofsky, Hepburn, Hayes, Hagerman, & Rogers, 2004). Therefore, the assessment strategy should include standardized measures of expressive and receptive language, as well as some activities involving imitation and praxis. In a person with Angelman syndrome, one might expect less interest in faces, and fewer initiations of social contact in a child with co-occurring autism (Bonati et al., 2007). Therefore, the assessment strategy should include ample opportunities for unstructured rime, so that the individual has the chance to initiate social interactions with others. More examples of potential areas for further assessment per syndrome are presented in Table 9.4.

2.2.6. Assess evenness and generalization of skills—Autism often presents with areas of strength and weakness (Schreibman, 1988). This splintering of skills may vary across skill domains, settings, situations, and people. Therefore, it is important to examine the child's behavior in both structured and unstructured situations so a complete understanding of the individual's abilities. During structured activities, such as developmental testing using a measure such as the Mullen Scales of Early Learning (Mullen, 1995) or the Bayley-III (Bayley, 2006), relevant clinical data can be obtained from observing how well the child can follow directions, orient to people, play appropriately, and attempt to copy the actions of another person. In unstructured situations, it has been clinically relevant in our work to observe the child's attempts to initiate social and communicative behaviors, as well as his or her attempts to respond to the bids of others. In our experience, one of the differentiators of co-occurring ASD from a general developmental delay is whether or not the child tries to engage socially and communicatively, not so much if their behavior is well coordinated and executed.

2.2.7. Examine social motivation—Many children with a developmental delay (without autism) demonstrate less complex, more immature, and more poorly integrated social and communicative behaviors than their typically developing peers, but they engage in these behaviors with appropriate affect and an underlying social orientation toward affiliation with their social partner (Sigman & Ruskin, 1999; Wishart, 2007). The differential identification of a co-occurring ASD may be less about social and communication proficiency and more about social motivation and where the child directs his or her neurological resources. For example, in our recent study, many parents of children with Down syndrome and ASD described that the child's most sophisticated problem-solving behaviors are related to avoiding social contact or minimizing active engagement in a shared experience (Hepburn, Fidler, & Lee, 2011). Conversely, children with Down syndrome without ASD have been noted to develop relatively sophisticated strategies for socially recruiting others to solve instrumental challenges faced in play (Fidler, 2005).

2.2.8. Consider the child's temperament—In our experience, children with known developmental disabilities who are referred for evaluations of autism symptoms are likely to

present with a somewhat difficult temperament. Sometimes they meet criteria for ASD, and sometimes the concerns expressed by their caregivers are best explained by an extreme behavioral style. A behaviorally inhibited, shy or anxious child may be misidentified as having a pervasive disorder of social-communication, and it is critical to plan the assessment procedures in order to minimize the impact of temperamental tendencies on observable behaviors. For children who may be anxious, shy, or sensitive to small changes in their environment, it can be very helpful to plan for extended warm-up time to clinic rooms and materials. Pacing sessions slowly to allow for adjustment to transitions and including parents, siblings, and other familiar people in the assessment session can help to establish a secure and comforting environment. Alternating activities by novelty and intensity of stimulation can also allow for direct observation of a child's self-regulatory behaviors. As in any child-focused evaluation, providing some exposure to new activities and tasks in order to assess how well a child responds to novelty can be informative. However, when testing any child who may be sensitive or highly reactive, it is equally important to monitor the child's level of distress and provide distracters, a change in setting, a motor break, or another diversion to maintain a positive rapport with the child.

2.2.9. Obtain a comprehensive medical history—Consider the child's experiences with illness and health care. For example, a young child with Down syndrome and leukemia may have experienced several intrusive and painful medical procedures in the first few years of his or her lifetime. These experiences could engender shyness in clinical offices of any kind, reticence in new places, not because of social withdrawal but due to wariness informed by experience. A young child with this history could present as exceedingly withdrawn in clinic, but also be reported to be quite animated and socially engaged in familiar settings (J. Browne, personal communication). When evaluating a child with this history, observations in multiple settings may be particularly important.

2.3 Collaborating with the family throughout the evaluation process

As with any evaluation of a possible developmental disability, it is critical to involve the family in the assessment process, both for data gathering and for interpretation of results. Actively involving the family in the evaluation allows for a clearer flow of information between the clinicians and the parents (Lord & Richler, 2006). In this section, we will address a few considerations that are relevant to involving the family in this evaluation process.

2.3.1. Adopt a transparent style of assessment—“Transparency” refers to the clinical practice of explicidy and honestly narrating the tasks administered, describing observations, and commenting on both strengths and areas of need throughout the clinical encounter. Establishing a transparent clinical approach can help to build the foundation for a more collaborative experience for the family (Shea, 1993), which may lead to improved understanding of the findings and attributions of credibility for the recommendations. In this model of transparent assessment, information is rolled out slowly, shared and reflected by the clinician by checking in with parents during observations (i.e., “Is this what you might see at home too?”), as well as at the conclusion of a particular assessment activity (i.e., “Was there anything that your son did during that activity that surprised you? Are there

things you have seen him do in more familiar places that we haven't been able to see here today?"). With this approach, the interpretative conference at the conclusion of the evaluation becomes a continuation of a dialogue that was initiated upon intake, and there should be few surprises for the family in this feedback session.

2.3.2. Focus on the referral question—Most likely, families seeking an evaluation for a co-occurring ASD are facing some challenges or stressors that intuitively are not explained by the identification of the genetic condition associated with intellectual and/or developmental disabilities. For some reason (or reasons), someone in the child's life thinks there is something "different" about the person's development, response to intervention, or overall profile that cannot be attributed to the underlying genetic condition and requires further examination. Understanding the nature of these concerns informs the assessment process and may even help with the differential diagnosis. For example, if a 9-year-old girl with Down syndrome is having trouble making and keeping friends, parents may become concerned that their child has social problems, which perhaps they did not anticipate in a child with a condition that is associated with a friendly demeanor and affiliative tendencies. If this child has fairly good nonverbal communication, directs affect, shares interests, imitates others, plays in a manner that is commensurate with her overall developmental level, attempts to initiate and respond to others, and can demonstrate social reciprocity (at least in some situations with some people), then the social difficulties may be related to social skills deficits or temperamental factors, and not indicative of a qualitative impairment in core social relating. Differentiating underdeveloped social skills from autism may not be in the parent's repertoire, and an informed clinician can assist in interpreting this distinction and recommending interventions. Conversely, if the parents report that their 9 year old with Down syndrome does not attempt to communicate with directed eye gaze, gestures, or vocalizations, rarely engages in sustained interactions with others, seems more interested in objects than people, and seems to be "in her own world"—then it is less likely that the child's social challenges reflect a lack of social skills, but rather signal a possible impairment in core social relating, which may be attributable to a co-occurring ASD. Simply asking the family members why they are seeking an evaluation at this time can be very informative.

2.3.3. Be aware of possible transference issues—Behaviorally defined diagnoses, such as an ASD, are always, to some extent, representative of an informed opinion that is of greater or less validity, depending upon a number of factors including the level of experience of the diagnostician, the behavior and mood of the child and/or parent during the assessment, as well as immediate human factors that impact decision making (Stone et al., 1999). For example, like in any clinical encounter, a well-meaning and experienced diagnostician may experience a high degree of personal identification and connection with the child or family member, and may unwittingly apply a subtle positive reframe to the concerning behaviors she or he witnesses as a result. In this situation, unintentional biases may develop that can delay identification.

Instances of possible co-occurrence of ASD in the context of a known genetic condition impacting intellectual functioning is, in our opinion, particularly vulnerable to clinician discomfort, given the background of ambiguity and the relative difficulty teasing apart

autism from a known intellectual disability (as opposed to identifying autism when the comparison group is typically developing children). Not only is the identification likely to be less certain, furthermore, the clinician may perceive a reignition of grief on the part of the family at the mention of a potential additional diagnosis. This subjective experience may increase a clinician's reticence to assess for autism symptoms. Clinicians must take care to monitor their own emotional reactions to the findings of the assessment and the challenges of interpreting them to families. Tolerating the discomfort of delivering difficult, but necessary news, is an important clinical skill to hone in this particular clinical context.

2.3.4. Ask families what their hopes and fears are regarding the possibility of another diagnosis—Some families will be uncomfortable with the additional identification and may view it as stigmatizing. Some parents report fearing that others will underestimate their child and will not provide enough challenge or set expectations high enough if there is a second diagnosis of autism. Others may be concerned that the additional identification could impact their access to insurance or medical care.

On the other hand, the additional identification of an ASD could result in potentially beneficial changes in the approach to a child's educational or therapeutic program. In some communities, the additional diagnosis may have practical implications for qualification for particular programs or services. This information could also help family members to form developmentally appropriate expectations and attributions for the child's perplexing behaviors (i.e., differentiating what the person currently “can't do” versus “won't do”). Another advantage of sharing the additional diagnosis with the family is that it provides information that may be relevant to genetic risks for other family members.

It is not uncommon for different family members to feel differently about the potential of a second diagnosis, or for family members and professionals in the child's life to differ in this regard. For the clinical evaluator, generating awareness of these varying perspectives is important, not because it changes the outcome of the differential diagnosis, but rather because it impacts how the clinician will deliver the findings and subsequent recommendations. In our practice, we do not try to “convince” a parent that a child has or doesn't have an ASD; rather, we endeavor to evaluate the person comprehensively and communicate our impressions in a clear manner. It is up to the parents and family to determine whether or not the conceptualization fits and how or if they will share the report with providers or consider implementing the recommendations. Sometimes more than one interpretative conference is needed to communicate across family members. Whenever possible, collaborating with educational/vocational teams, primary care physicians, and other service providers can also help to support delivery of appropriate interventions.

3. Implications for Intervention

Empirical research on the effectiveness of interventions that have been developed and studied in children with autism has not yet been systematically conducted in children with known genetic conditions and co-occurring autism. Such research is needed, particularly in the areas of social and communication interventions. With that caveat in mind, we have

developed the following implications for intervention, based upon our clinical experience and the existing clinical literature.

3.1 Consider implementing interventions designed specifically for persons with ASD

There are comprehensive intervention programs, such as Early Start Denver Model (Rogers & Dawson, 2009), SCERTS (Prizant, Wetherby, Rubin, Laurent, & Rydell, 2006a, b), Pivotal Response Training (PRT; Koegel & Koegel, 2006), and TEACCH (Mesibov, Shea, & Schopler, 2005) to consider integrating into the treatment plan. Instructional approaches grounded in principles of Applied Behavior Analysis (ABA) (i.e., systematic teaching, relying upon data on child performance to dynamically adjust instructional procedures) are thought to be efficacious in intervention for autism (Committee on Educational Interventions for Children widi Autism, National Research Council, 2001) and should be integrated into the child's programming. Although many of these interventions have not been explicitly researched in children with more than one diagnosis, careful implementation with ongoing monitoring of progress is certainly within the bounds of appropriate practice.

3.2 Focus intervention efforts on building communicative intention

Clinical experience suggests that a child with co-occurring autism may benefit from therapeutic focus on building intentional communications, usually beginning with requesting. Using communicative temptations, as described by Prizant et al. (2006b), and providing practice requesting across settings and people can be helpful for building a nonverbal communicative repertoire. Developing communicative competence can also reduce the frequency and intensity of problem behaviors.

3.3 Explicitly teach joint attention, imitation, and play in a variety of instructional formats

These three skills are thought to be foundational skills for social learning and need to be taught deliberately to many persons with ASD. Providing frequent opportunities for 1:1 instruction of pivotal social skills is essential, and many persons with ASD and a known genetic disorder will not acquire new skills as efficiently in group contexts. While teaching these skills in more controlled instructional contexts, it is also important to continually practice the use of these skills in other social contexts, such as within small groups of peers, in the community, home, and classroom.

3.4 Consider the person's learning style and adjust the instructional approach accordingly

Although learning style is a highly individualized characteristic, many persons with ASD present with somewhat predictable learning differences, which ought to be assessed on an individual basis. For example, many persons with ASD do not learn well through natural learning opportunities without explicit instruction and need to be actively taught new skills with a lot of repetition and practice across settings. Some children with ASD do not respond positively to praise, but are more motivated by sensory rewards or opportunities to escape from demands. Some have difficulty with transitions between activities and benefit from a transition routine and/or requiring fewer transitions throughout a child's day.

3.5 Identify strengths and interests and integrate into the person's daily experiences

It is not known if the profile of relative strengths observed in many persons with ASD is also demonstrated in persons with an existing genetic syndrome; however, it is important to identify potential strengths. Specifically, it is helpful to determine if the person learns better through visual than auditory means, prefers routines, seeks familiarity, attends to details better than the “big picture,” and is more competent in self-directed, object-oriented tasks (such as completing a puzzle) than in cooperative, socially oriented activities (such as dramatic play). Some children with ASD solve nonverbal, visual-spatial problems much more competently than verbally mediated problems. If this is the case, then instruction and leisure focused on building upon these existing strengths is as important to pursue as the interventions designed to ameliorate relative weaknesses. Many children with ASD develop a strong, focused interest (e.g., a favorite Disney character or an interest in trains). This interest can be integrated into learning activities (such as learning to count using a toy train set), or can be utilized as a reward for persisting in a new task.

3.6 Explore technology to facilitate communication, literacy, social understanding, cognitive focus, and personal safety

Assistive technology devices can be quite helpful in promoting communication and building literacy (Goodwin, 2008). Computerized instruction can be particularly motivating for children who do not naturally learn well in social groups and prefer visual stimulation and predictive teaching sequences (Williams, Wright, Callaghan, & Coughlan, 2002). Video modeling (i.e., showing the child a short film to clarify what to expect in an upcoming novel event or how to behave in a certain situation) has been shown to be potentially efficacious for many learners with ASD (Buggey, 2009; Rayner, Denholm, & Sigafoos, 2009). Wristbands with GPS technology are extremely helpful for persons who may wander away from caregivers.

3.7 Teach self-care, independent leisure skills, and community safety through routines, practice, and explicit instruction on a dally basis across settings

Educational programming should include functional, adaptive skills in addition to academic, social, and communicative targets. Developing and practicing routines for daily activities, such as mealtime, bedtime, toileting, going to school/work are very important for developing independence. Repetition, predictability, and structure can help to promote more child engagement in daily activities.

3.8 Provide parent training in natural settings

Families may face many different challenges in raising a child with a complex presentation. Helping parents to adopt consistent, adaptive routines, incorporate visual and physical structure into the home, create opportunities for communication and social engagement, prevent problem behaviors, and build independence in self-care are all potential targets of family focused intervention. Several parent education programs exist that could be quite helpful for families of children with dual diagnoses. Examples include Responsive Teaching (Mahoney, Perales, Wiggers, & Herman, 2006), Early Start Denver Model (Rogers & Dawson, 2009), Education and Skills Training Programme for Parents (Brereton & Tonge,

2005), and PLAY Project Home Consultation Program (Solomon, Necheles, Ferch, & Bruckman, 2007).

4. Concluding Comments

In conclusion, phenotypic research is proceeding across several genetic disorders, and variations of the autism phenotype are being described in clinical studies of chromosomal conditions, such as Down syndrome, X-linked conditions, such as fragile X syndrome, and several relatively rare, but disabling disorders, such as tuberous sclerosis, Cornelia de Lange syndrome, and Angelman syndrome. Research concerning the co-occurrence of ASD and specific genetic conditions may inform our understanding of the neurobiology of developmental disorders, and may provide important clues for prevention and intervention.

Conducting an evaluation for autism symptoms in a person with a known genetic syndrome associated with an intellectual or developmental disability is a challenging clinical endeavor. Approaching the evaluation within a developmental framework, applying evidence-based practices of assessment, and actively involving the family in the process are recommended. Although identification of an additional condition can be very difficult for some families, others report feeling some relief in understanding why their son or daughter seems different from his or her peers with the same genetic condition. More research is needed to evaluate the impact of interventions with complex children; however, identification of an ASD could facilitate delivery of appropriate educational or therapeutic services and may promote adaptive adjustment for family members.

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Table 9.1

Clinical observations and related literature concerning autism phenotype by syndrome

Syndrome	Key differentiating characteristics[a]	References
Down syndrome	*Core relatedness*: Children who also have ASD usually show notable difficulty responding to social bids from others and are less likely to be oriented toward people than objects *Intentional communication*: Children who also have ASD demonstrate fewer attempts to use nonverbal strategies to indicate wants or needs. Often, if misunderstood, the child with ASD makes few attempts to try another method of communication *Sharing affect*: Children who also have ASD rarely direct a variety of facial expressions toward others to communicate affect *Initiating functional activities*: Children who also have ASD are often described by their parents as preferring to play in repetitive, stimulatory ways, instead of developing doll play and other social and independent play activities	Bregman and Volkmar (1988), Capone, Grados, Kaufinann, Bernard-Ripoll, and Jewell (2005), Dykens (2007), Ghaziuddin, Tsai, and Ghaziuddin (1992), Hepburn, Philofsky, Fidler, and Rogers (2008), Hickey and Patterson (2006), Kent, Evans, Paul, and Sharp (1999), Kuschner (2010), Lowenthal, Mercadante, Belisario, Piloto, and Paula (2010), Molloy et al. (2009), Paley and Hurley (2002), Rasmussen, Borjesson, Wentz, and Gillberg (2001), Reilly (2009), Starr, Berument, Tomlins, Papanikolaou, and Rutter (2005)
Williams syndrome	*Emotional contagion*: Children with ASD may be less likely to "catch" the facial expressions and affect of a social partner within the natural flow of an interaction *Functional imitation*: Spontaneous imitation is often a strength for children with WMS without ASD. *Social play*: Social content in spontaneous play is less likely to be observed in children with WMS and ASD *Frequency of social initiations*: There is some evidence suggesting fewer social initiations (particularly for purely social purposes) in children with both WMS and ASD *Quality of social responses*: Although many children with WMS often use "scripted" or stereotyped statements in interactions, those without ASD tend to pair nonverbal behaviors (such as eye gaze, facial expressions) with social responses, thus creating a sense of connectedness even when verbal content is somewhat restricted in generativity	Fidler, Hepburn, Most, Philofsky, and Rogers (2007), Klein-Tasman, Phillips, Lord, Mervis, and Gallo (2009), Lacroix, Guidetti, Roge, and Reilly (2009), Philofsky, Fidler, and Hepburn (2007), Semel and Rosner (2003), Sullivan and Tager-Husberg(1999),Tager-Rusberg, Skwerer, and Joseph (2006)
Angleman syndrome	*Soothability by social contact*: Individuals with Angelman syndrome are often soothed by social/physical contact by another person, regardless of the familiarity of the social partner. Those with co-occurring ASD may not be as easily soothed by social contact *Attempts to interact socially*: There is some evidence to suggest that individuals with Angleman syndrome without ASD are more likely to physically approach others, remain in close physical proximity, and initiate simple social games than their peers with Angelman syndrome and ASD *Emotional contagion*: Some clinicians suggest that individuals with Angleman syndrome without ASD are more capable of spontaneously "catching" and mimicking facial expressions than those with both conditions	Peters, Beaudit, Madduri, and Bacino (2004), Trillingsgaard and Ostergaard (2004), Walz (2007)
Fragile X Syndrome	*Overall intellectual functioning*: Children with FXS and ASD tend CO show greater intellectual impairment *Receptive language skills*: Children with FXS and ASD tend to show greater impairments in receptive abilities. *Imitationskills*: Imitation is often a relative strength in children with FXS without ASD. *Social orienting*: Although gaze aversion is often observed in persons with FXS regardless of autism status, those with cooccurring ASD tend to not improve their social orienting with familiarity and time within an interaction, while those with FXS without ASD may show improved social orienting across an interaction	Bailey et al. (2001), Cohen et al. (1991), Cornish, Turk, and Hagerman (2008), Demark, Feldman, and Holden (2003), Dissanayake, Bui, Bulhak-Paterson, Huggins, and Loesch (2009), Kaufinann et al. (2004), McDuffie et al. (2010), Philofsky et al. (2004), Reiss and Freund (1990)

[a] Relative to peers with the same syndrome without autism.

Table 9.2

Estimated rates of developmental progress per syndrome with and without ASD[a]

Syndrome	Developmental progress in persons without co-occurring ASD	Developmental progress in persons with co-occurring ASD
Down syndrome	3–4 months per 12 months	1–2 months per 12 months
Williams syndrome	5–10 months per 12 months	1–4 months per 12 months
Angelman syndrome	2–4 months per 12 months	1–2 months per 12 months
Fragile X syndrome	5–11 months per 12 months	1–4 months per 12 months

[a]Bailey et al. (2001), Capone, Grados, Aylward, and Hunt (1990), DiGuiseppi et al. (2010), Dissanayake et al. (2009), Lo-Castro et al. (2010), Molloy et al. (2009), Moss and Howlin (2009), Peters. Beaudit, Madduri, and Bacino (2004).

Table 9.3

Developmental sequence of appropriate social behaviors by developmental level

Social behaviors	Expected age of accomplishment
Expresses a variety of emotions (including happiness, sadness, interest, surprise, anger, fear, disgust)	By the age of 6 months
Demonstrates a predictable social smile (i.e, smile that is clearly directed or shared with another person)	By the age of 6 months
Matches the emotions expressed by an adult in face-to-face interactions	By the age of 6 months
Shows nervousness with strangers (and therefore is differentiating familiar and unfamiliar people)	Between 7 and 12 months
Relies on caregiver to be a secure base while exploring environment	Between 7 and 12 months
Uses social referencing (looking back at caregiver) in order to pick up cues about how to react in new situations	Between 7 and 12 months
Readily joins in play with familiar children, such as siblings, cousins, and so on	Between 13 and 18 months
Recognizes image of self in mirrors and pictures	Between 13 and 18 months
Begins to show empathy for others (by trying to comfort others or directing sympathetic facial expressions to others who are hurt or unhappy)	Between 13 and 18 months
Able to follow simple directions given by familiar caregiver	Between 13 and 18 months
Expresses more subde, more complex emotions, such as shame and embarrassment	Between 19 and 24 months
Verbally expresses a variety of emotion words	Between 19 and 24 months
Begins to use communication as a tool for self-regulation	Between 19 and 24 months
Uses own name and personal pronouns	Between 19 and 24 months
Understands basic categories that are associated with people, such as age and sex	Between 19 and 24 months
Distinguishes between intentional and unintentional acts by self and others	Between 2 and 3 years
Shows ability to be cooperative with caregivers	Between 2 and 3 years
Shows emerging understanding of how actions cause feelings and vice versa	Between 2 and 3 years
Expression of complex emotions (such as shame, embarrassment, guilt, pride) increases	Between 3 and 5 years
Engages in first friendships	Between 3 and 5 years

Adapted from Berk (1996).

Table 9.4

Specific areas to assess in the differential diagnosis by syndrome

Genetic syndrome	Relative strengths in the absence of autism	Tools to assess these areas
Down syndrome	Social interest Frequent attempts to communicate Rich emotion sharing Frequent social initiations	•Communication and Symbolic Behavior Scales (Wetherby & Prizant, 2005) •Parent-child play •High affect, stimulating play •Screening for tool for autism in toddlers (STAT; Stone, Coonrod, Turner, & Pozdol, 2004)
Williams syndrome	Emotional contagion Social play Functional imitation Frequency of social initiations Quality of social responses Nature of pragmatic difficulties	•Birthday party from ADOS with surprise present added to play activity •Empathy tasks (see Yirmiya, Sigman, Kasari, & Mundy, 1992) •Children's Communication Checklist (Bishop, Chan, Adams, Hardey, & Weir, 2000) •Imitation activities from the STAT (Stone et al., 2004) or the ADOS (Lord, Rutter, DiLavore, & Risi, 1999)
Angleman syndrome	Soothability by social contact Attempts to interact socially Emotional contagion	•Parent-child play •Sensory-social routines from Early Start Denver Model (Rogers & Dawson, 2010) •High affect, stimulating play
Fragile X syndrome	Receptive language skills Imitation skills Social orienting Sensory reactivity	•Preschool Language Scales (PLS; Zimmerman, Steiner, & Pond, 2002) or Clinical Evaluation of Language Fundamentals (CELF; Semel, Wiig, & Secord, 2000), or another standardized assessment of language that includes both receptive and expressive language and has appropriate norms •Imitation items, either from the STAT or ADOS •Birthday party from the ADOS, with surprise present added to routine •Short Sensory Profile (Mcintosh, Miller, Shyu, & Dunn, 1999)