Annual Research Review: Re-thinking the classification of autism spectrum disorders

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Background: The nosology of autism spectrum disorders (ASD) is at a critical point in history as the field seeks to better define dimensions of social-communication deficits and restricted/repetitive behaviors on an individual level for both clinical and neurobiological purposes. These different dimensions also suggest an increasing need for quantitative measures that accurately map their differences, independent of developmental factors such as age, language level and IQ. **Method:** Psychometric measures, clinical observation as well as genetic, neurobiological and physiological research from toddlers, children and adults with ASD are reviewed. **Results:** The question of how to conceptualize ASDs along dimensions versus categories is discussed within the nosology of autism and the proposed changes to the DSM-5 and ICD-11. Differences across development are incorporated into the new classification frameworks. **Conclusions:** It is crucial to balance the needs of clinical practice in ASD diagnostic systems, with neurobiologically based theories that address the associations between social-communication and restricted/repetitive dimensions in individuals. Clarifying terminology, improving description of the core features of ASD and other dimensions that interact with them and providing more valid and reliable ways to quantify them, both for research and clinical purposes, will move forward both practice and science. **Keywords:** Autism spectrum disorders, dimensions, classification, diagnosis, DSM-IV, DSM-5, development.

Introduction

As we move into new editions of the major frameworks for diagnosing autism, the Diagnostic and Statistical Manual (DSM-5) of the American Psychiatry Association (2012) and the International Classification of Diseases (ICD-11) of the World Health Organization (2012); (see also Rutter, 2011), proposals for classifications of autism and related disorders (referred to interchangeably as autism, autism spectrum disorders or ASD) are well underway but not finalized. Now is a time to consider some of the challenges we face in the nosology of ASD. The focus of this review is on issues related to diagnostic classifications in ASD, including a selective discussion of how these issues may be addressed in the proposed new classification frameworks. Full descriptions of these new systems from their respective entities will be available when they are published.

The review is organized in four sections. First, challenges to existing (DSM IV; ICD-10) ASD classifications are discussed starting with general issues in the diagnosis of psychiatric and psychological disorders. This includes differences between concepts of disease and disorder, as well as diagnosis, and the role of dimensions as a useful construct for clinical purposes and for neuroscience. Second are sections that discuss the core dimensions that underlie a category of ASD. Third, specific changes proposed in

DSM-5 and ICD-11are outlined. Finally, we come back to questions of classification, description and measurement in terms of clinical needs and links to neurobiological research.

Issues in classification: diseases or disorders?

Existing diagnostic frameworks for ASD (American Psychiatric Association, 1987, 2000) occur within classification systems for diseases, defined as an abnormal condition or risk for which there is a known etiology or pathophysiology (Hyman, 2010; Kraemer, 2008). Concepts of disease have been an underpinning of modern medicine since the late 1880s, with the expectation that disease can be prevented or if contracted, treated and cured (Stewart & Devlin, 2006; Sykes, 2001). However, conceptualizations of psychiatric and psychological disorders moved beyond this model many years ago (Susser, Brown, & Matte, 1999). Because a high proportion of health concerns in many countries are associated with chronic conditions and complex interactions among genetic and environmental factors, rather than infectious diseases, there is increased insistence that other branches of modern medicine do the same. Nevertheless, the urge to consider psychiatric and psychological disorders as 'diseases' remains extremely powerful (Hyman, 2010), perhaps assuming that conceptualizing psychiatric disorders as diseases means that there will be simple etiologies and pathophysiologies that can be used to treat, cure and/or prevent them.

Relatively independent of the existing diagnostic systems, for the last 30 years or so, hope for understanding autism has lain in genetic and neurobiological approaches that might identify or lead to clear etiologies. Expectations have been high, with predictions of the ability to soon account for 30–40 percent (Geschwind, 2011) of cases of autism through identifiable genetic variation. From this point of view, studies of behavior have been treated as being valuable primarily as providing quantifiable measures that can be linked to potential biomarkers that provide objective, and biologically meaningful associations to underlying pathophysiology or strong risk factors (Lee et al., 2010).

Surprisingly, the most significant scientific challenge to the concept of autism as one 'disease' or even 'diseases' is the heterogeneity of the genetic findings (Veenstra-Vanderweele, Christian, & Cook, 2004). Not only are many different genetic patterns associated, at some level, with autism, but also many of these same patterns are associated with numerous other psychological and psychiatric disorders (Guilmatre et al., 2009). Because of the lack of an 'autism gene' and the poor specificity of the genetic findings, the spotlight has shifted from providing genetic etiologies for all or most individuals with autism to describing small subsets of individuals with shared genetic risk and attempting to link the risk to dimensions of behaviors (Geschwind, 2011) or describing general but varied genetic phenomena, such as large, rare de novo copy number variants and investigating the association between the number of genes affected and features related to autism, such as intelligence (Sanders et al., 2011). These approaches provide important new leads that require us to move beyond earlier expectations of simple correspondence between having autism and having a very specific genetic abnormality.

Consequently, while genetic descriptions will doubtless be important, in the immediate future, reference to a genetic finding such as a 16p11.2 deletion or a 15q11–13 duplication, is an important addition to, but in no way a replacement for a behavioral diagnosis because the links to autism, while strong, are not unique or universal (Walsh & Bracken, 2011). In order to access the information typically associated with a diagnosis (e.g., course, response to treatment, risk factors, associated conditions), one still has to come back to behavior. For families learning about their child's diagnosis, educators and therapists developing individualized programs, individuals with ASD seeking to understand their own strengths and challenges, and investigators developing new non-medical interventions, behavioral conceptualizations remain critical (Charman et al., 2011; Shattuck et al., 2009).

Neuroimaging, both structural and functional studies, and other methods of neurophysiology (Jeste & Nelson, 2009; Nelson & McCleery, 2008) have been another source of hope for understanding ASD-specific mechanisms of brain function to identify links between etiology and behavior. Initial studies of brain structure showed increased total brain (Piven, Arndt, Bailey, & Andreasen, 1996) as well as amygdala (Sparks et al., 2002) and cerebellum (Piven, Saliba, Bailey, & Arndt, 1997) volume. Structural studies have shown correlations between brain structures and symptom severity (Schumann, Barnes, Lord & Courchesne, 2009). However, there has been difficulty replicating these findings mostly due to small sample sizes, and variability in ages across studies. Longitudinal volumetric studies have provided greater insight into potential varied trajectories of brain development in autism (Hazlett et al., 2011; Mosconi et al., 2009). In addition to the structural studies, functional imaging has targeted ASD phenotypes, using tasks that probe social difficulties inherent to ASD such as looking at faces (Dalton et al., 2005), or language processing paradigms (Harris et al., 2006) and have shown abnormal patterns of activity in individuals with ASD. Claims of near-perfect identification of individuals with ASD through imaging algorithms (Ecker et al., 2010) and of clear discriminability of children at risk for autism have been made (Hughes, 2010). Yet, these approaches seldom provide data on an individual level, do not yet have well-accepted standards for replicability across time or site (Lotspeich et al., 2004) and have rarely addressed questions of specificity of findings to ASD. Thus, it is early to build diagnostic systems from structural and functional neuroimaging measurements.

In neurobiology, measurement of a dimension provides both a way to use quantitative analyses that offer additional statistical power beyond categories and to include more subjects in research studies, because milder cases or even non-cases with some symptoms can be included (Ronald, Larsson, Anckarsater, & Lichtenstein, 2011). Additionally, dimensions offer important theoretical underpinnings to posited links to neurobiology, such as mechanisms of the social brain (Pelphrey, Shultz, Hudac, & Vander Wyk, 2011) and certain forms of anxiety (Juranek et al., 2006; Kleinhans et al., 2010). Thus, the concept of *dimension* is crucial to the reorganization of DSM-5 (http://www.dsm5.org) and to ICD 11. Based on results both from genetics and from neuroscience, the assumption has been that, when we have a good, or several good, biomarkers, the behaviors that comprise a diagnostic syndrome will be of less importance than easily measurable 'dimensions' of behavior. From this perspective, links can be made straight from biology (biomarker of etiology used in nosology) to biology (neuropathophysiology) to biology (medical treatment) of a dimension, even if we cannot recommend an effective treatment for all core diagnostic features (see Figure 1).

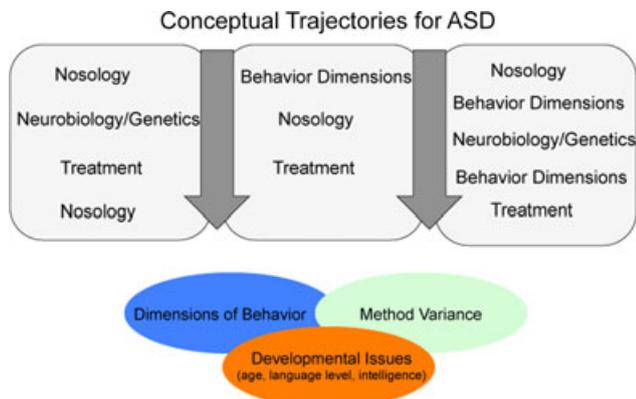Recently, studies of functional neural changes associated with genetic variation have become more

Figure 1 Illustration of the different conceptual trajectories for the nosology of autism spectrum disorders. The variables of 'dimensions of behavior', 'method variance' and 'developmental issues' all have significant contributions and must be incorporated and/or considered in any classification of autism

common with the hope of providing greater insight into the biology of ASD (Scott-Van Zeeland et al., 2010). However, small sample sizes and a lack of specificity to behavioral dimensions make this research still somewhat limited. Often, nonspecific questionnaires such as the Social Responsiveness Scale, which measures far more than autism-specific social deficits (J. S. Anderson et al., 2011) or summary scores from measures with limited validity in terms of equivalence of the dimensions that define autism (Vaidya et al., 2011) have been used as correlates with brain function. Importantly, neuroimaging studies have begun to move beyond analyses that compare a group of 'healthy' participants to those with autism, to including additional comparisons such as those with ADHD or language impairments (see Brieber et al., 2007; Malisza et al., 2011). The question of specificity to ASD, in contrast to other disorders, is particularly important if the focus is on earlier or better diagnosis. Studies with healthy controls can contribute to theoretical understanding of neurobiological underpinnings, but ultimately we do want to link the neurobiology to the behaviors that we are trying to explain in ASD, not just to the presence of some kind of disorder or impairment. Particularly given our gradual understanding of the role of learning and experience, the need to take into the account different experiences and their interactions with developmental differences through targeted comparisons of carefully selected samples is very important. Overall, care needs to be taken to avoid prioritizing imaging results over behavior or prioritizing behaviors that happen to fit well into imaging studies as key concepts on which to build diagnostic models of ASD so that they can fit into imaging, or genetic studies. Such strategies may promote research directions that are ultimately less useful for understanding underlying core ASD pathophysiologies or etiologies. Valid patterns of brain function that are associated with reliably measured behavioral dimensions of ASD, even when

reliable, if they do not discriminate children with autism from children with other disorders and if they are not predictable on an individual level, a behavioral diagnosis would still be needed. This behavioral diagnosis would be needed to not only describe the severity of features within ASD but other dimensions of behavior, as discussed below.

Arguing for the exclusive use of categories or of dimensions creates a false dichotomy. Dimensions can always be made into categories by defining thresholds and, as we see with the existing DSM-IV and ICD-10 and the proposed DSM-5 and ICD 11 criteria, categories are formed from dimensions (Pickles & Angold, 2003). In much of medicine, especially behavioral research, dimensions are comprised of items that each describes a category of behavior. Consequently, rather than contrasting categories versus dimensions, we might more usefully ask, for what purpose do we define and measure dimensions: To more accurately describe, predict and be able to change behavior? OR to link with neurobiological findings? And how does what are the relationships among diagnostic descriptions (often reflecting different behaviors or behavioral categories), dimensions and categories, such as disorders?

If we move to conceptualizations of neurobiological pathways of development, rather than a disease that is present or not, the role of dimensions shifts. Behavioral dimensions would serve as the indicators of the need for different services and of response to treatments, as well as risk for associated problems. Behavioral dimensions would also become the indicators of how neurobiological changes occur, how they are intermeshed and how developmental pathways might be modified or built upon (Cicchetti et al., 2011; Rutter & Sroufe, 2000). This more developmental approach would focus on change, and involve reconsidering the meaning of the rich, complex findings from genetics and to some degree, from neuroscience, based on categorical conceptions of ASD and very broad dimensions as they might be linked to more specific behavioral constructs. It would also require more attention to specificity of behaviors associated with ASD, and when nonspecific dimensions are of interest, their interactions with core features.

What should the behavioral dimensions for ASD be?

The two major existing diagnostic frameworks for ASD, DSM-IV and ICD-10, both describe three defining dimensions of behavior: 1) deficits in social reciprocity, 2) deficits in communication and 3) presence of restricted, repetitive behaviors and interests. However, as shown in Figure 2, ASD definitions in both new systems, DSM-5 and ICD-11, contain only two domains: (1) social communication/social interaction and (2) restricted, repetitive behaviors and interests (http://www.DSM5.org;
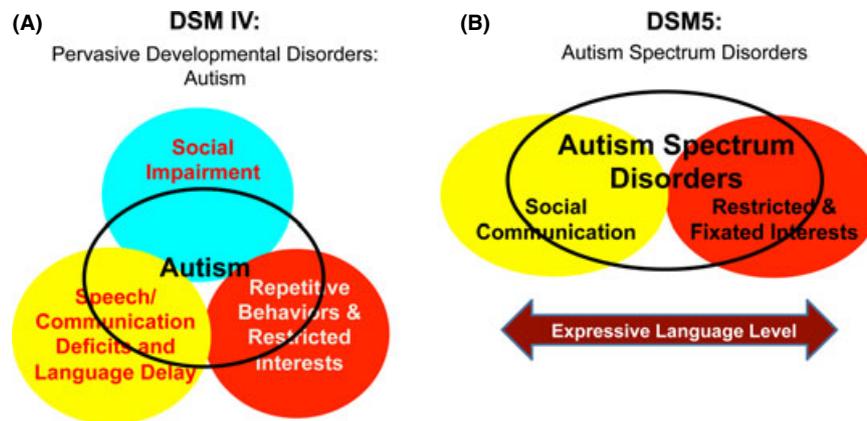
Figure 2 (A) Existing diagnostic classification according to the DSM-IV for Pervasive Developmental Disorders. (B) Proposed DSM-5 classification dimensions for autism spectrum disorders

World Health Organization, 2012). These changes reflect a substantial literature that has shown that, in many cases, whether a particular behavior is classified under social or communication domains is arbitrary (Gotham, Risi, Pickles, & Lord, 2007). For example, nonverbal behaviors such as eye contact, gesture and facial expression are social and communicative; conversation is a social use of language. Many factor analytic studies of children with ASD showed one social-communication factor (Gotham et al., 2007). An exception was one factor analytic study of children with ASD that gave all children who did not speak 'severe' scores on all communicative items (such that a child who was nonverbal would have received scores of severe deficits on pronoun reversals, stereotyped speech and conversation) (Tadevosyan-Leyfer et al., 2003). Though structural language skills are not a defining core feature of ASD in the new systems, they remain a crucial dimension in both clinical decision-making and as a target for neurobiological research.

Where should the dimension of language skill fit into classification of ASD?

The argument for considering language delay as a separate dimension that is not part of ASD diagnostic criteria, but critical to how those diagnostic criteria are used, is two-fold. First, language delay is not specific to autism (Bishop & Norbury, 2002). By far the majority of young children referred for concerns about language delay do not have ASD or even severe developmental delays (Ellis & Thal, 2008), conversely, not all, though many children with ASD have language delays (Baird et al., 2008; Kjellmer, Hedvall, Fernell, Gillberg, & Norrelgen, 2012). By later school years, many children with ASD are fluent speakers (Smith, Mirenda, & Zaidman-Zait, 2007). Current language level (at a given point in time, how a child uses language) and relative degree of language delay (how a child or adult's expressive or receptive language skills compare to others of the

same age) play significant roles in the diagnosis and the course and treatment of ASD (Anderson, Maye, & Lord, 2011). Diagnostic features vary markedly depending on a child or adult's expressive language (Gotham et al., 2007). Several studies have also suggested that significant delays in receptive language, compared to other skills, discriminate children with ASD from those with other communication or developmental patterns (Philofsky, Hepburn, Hayes, Hagerman, & Rogers, 2004). Other research has suggested that many different measures of language skill in ASD, such as receptive and expressive language, vocabulary and syntax are often highly correlated (R. J. Luyster, Kadlec, Carter, & Tager-Flusberg, 2008). In addition, within ASD, current expressive, and even more so, receptive language scores are also highly correlated with both nonverbal IQ and full-scale IQ (which includes verbal IQ, so this is not surprising) (Luyster et al., 2008); this is discussed further below.

Other perspectives are also important concerning the role of communication, often defined in terms of language skills within verbally fluent children with ASD. Twin and population studies using parent questionnaires that broadly describe autistic-like difficulties relevant to children of average intelligence have continued to find somewhat different genetic patterns, with social, communication and fixated interests following different paths (Robinson et al., 2011; Ronald et al., 2006). Bishop (2003) has argued for a continuum of semantic and pragmatic difficulties that merge into ASD conceptualizations. Such findings challenge us to consider more carefully how the social and other deficits associated with ASD interact to affect particular components of language development, and perhaps to provide more precise consideration of different aspects of language. Nevertheless, language level, often summarized by a child or adult's current level of expressive language is a crucial dimension in the diagnosis of ASD that needs to be considered separately in its own right, and as it affects ASD symptoms.

For the newly proposed diagnostic systems, one outcome of the decision to move away from a separate factor of language and communication is that social examples of both nonverbal (e.g., use of gaze; gestures) and language (e.g., 'chat,' conversation) are now included within social communication/social interaction as are social aspects of imaginative play rather than within a separate domain of communication. Repetitive aspects of language, such as stereotyped speech, delayed echolalia, repeated questions ('How tall were you when you were two?') and vocalizations, neologisms (calling a hairdryer a 'poomba'), verbal rituals (demanding that a mother count to five before putting on a shoe) and restricted aspects of play now fall within the second domain (see http://www.DSM5.org). This approach expands the possible examples of these dimensions. The intention, at least in DSM-5, is that all behaviors that contributed to the former dimension of communication, with the exception of overall language delay, would fall within either social-communication or under fixated interests/repetitive behaviors. The expectation is that, when DSM-5 criteria are used as intended, this will not change the number of individuals receiving valid diagnoses (Swedo et al., 2012) and that there would be no need for children and adults with existing ASD diagnoses to have to be re-diagnosed, given the expected comparability of the inclusiveness of the former and proposed systems.

The social-communication/social interaction dimension of ASD

Understanding the nature of social communication difficulties in ASD; can this general construct be unpacked into more meaningful dimensions?

Many authors have proposed qualitative social difficulties as the most universal and specific characteristics of ASD (Sigman, Dijamco, Gratier, & Rozga, 2004). Several papers by Lorna Wing and Judith Gould were particularly important in introducing the concept of a triad of deficits (social, language comprehension, imaginative play) that extended beyond classic autism (Wing & Gould, 1978) and in characterizing levels of severity of social deficits from aloofness to passivity to active, but odd socially-directed behavior (Wing & Gould, 1979). Twin studies also indicated that the social and other difficulties with autism, even within identical twin pairs, came in many forms (Folstein & Rutter, 1977).

The new diagnostic criteria in DSM-5 and ICD-11 propose three principles in defining diagnostic features within the social dimension: social-emotional reciprocity; nonverbal communicative behaviors used for social communication; deficits in developing and maintaining relationships (http://www.DSM5.org). To receive a diagnosis of ASD, an individual must show difficulty in use and/or understanding,

operationalized as at least one current example, within each of the three levels. Nonverbal communication deficits include areas such eye contact, body language, facial expression, gesture, and integration of language and nonverbal behaviors. Social reciprocity includes sharing of interests, conversation, turn taking, sharing of affect, and lack of initiation or social approach. Deficits in relationships include both adjusting behavior to suit different social contexts, sharing within imaginative play and difficulties forming and/or maintaining relationships appropriate to age and developmental level. Thus, they could be operationalized by a toddler's lack of interest in other children or his siblings all the way up to an adult who may have friendships but has never had an intimate relationship or who has trouble understanding the complexity of different roles within a work-context (see DSM-5.org). The specification of 'use' or 'understanding' is an important addition in the DSM-5 criteria.

Examples were selected on the basis of research findings, but it is important to note that the three subdomains are not empirically defined dimensions. Rather they are descriptions of the levels on which difficulties are typically manifested, with the goal of providing criteria with high sensitivity and specificity to ASD.

The literature documenting social behaviors and difficulties in ASD is extensive, and in contrast to much of the neurobiological research, notable in its consistency and replicability across studies. However, as seen in the clinical principles described above, empirically defining mechanisms that traverse age and development to underlie these unique patterns of behavior has been a challenge. Many of the most theoretically important constructs proposed as social deficits, such as theory of mind (Baron-Cohen, Leslie, & Frith, 1985), joint attention (Mundy, Sigman, & Kasari, 1990) and social motivation (Dawson, Webb, & McPartland, 2005) are striking in their presence at some ages and in some individuals but not observable in very young children or no longer present in significant numbers of older children or adults (Bowler, 1992; Gillespie-Lynch et al., 2012). Researchers have carried out many clever and interesting studies that highlight various aspects of social deficits (Jones, Carr, & Klin, 2008; Kaiser et al., 2010). However, empirically validated dimensions within social-communication that accurately differentiate ASD from other disorders vary greatly depending on the comparison population and the developmental level of the individual with ASD (S. Bishop, Gahagan, & Lord, 2007). When children who received clinical diagnoses of ASD were compared to children who received other diagnoses (and not ASD) but who also had high scores on a standard measures of ASD social reciprocity, the items that differentiated the two groups were basic social-communication behaviors, such as use of facial expression, communicating shared enjoyment,

eye contact and gestures (Lord, Storoschuk, Rutter, & Pickles, 1993), in contrast to more interactive skills, such as offering comfort or playing with peers. These findings suggest that nonverbal social-communication might be especially distinctive, but this has not been replicated in attempts to identify different social factors.

Other deficits in ASD may or may not be uniquely social but may have significant effects on social interactions. For example, children with ASD pay proportionately less attention to people than objects (Black, Freeman, & Montgomery, 1975) and spend less time, when not structured, doing anything that shows some intent or focus (Lord & MaGill-Evans, 1995). These findings call out for broader cognitive theories to underlie dimensions of social deficits across development and that might unite the important, but often age and language-related constructs such as joint attention and theory of mind, as well as ways of measuring concepts that span these theories (Hobson, 2002).

Subdomains within social deficits in ASD?

To date, measures of social deficits in ASD have not proved useful in dissecting a social factor into components. Though the Social Responsiveness Scale (SRS) provides clinical social summary scores, these scores are not empirically validated and not recommended for use in research (J.N. Constantino & Gruber, 2005). Attempts to group social and communication items, beyond pulling out expressive language level, in the major ASD measures, including the SRS, Autism Diagnostic Interview-Revised (ADI-R) (Rutter, Le Couteur, & Lord, 2003), Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 2000), 3di (Skuse et al., 2004) and Diagnostic Interview for Social Communication Disorders (DISCO) (S. R. Leekam, Libby, Wing, Gould, & Taylor, 2002) have not yet yielded stable, empirically validated, meaningful factors within the social area (Gotham et al., 2007; Kim & Lord, 2012b).

One possible approach in the search for different subdomains and dimensions within the social-communication construct is to consider the various levels of information provided by instruments developed with different purposes. Here, care must be taken because there is possible method variance, related to how an instrument is administered (e.g., questionnaire, interview), the type of response expected (yes/no, Likert scales) and the context of the question (presented as behavior problems, strengths, concerns). Nevertheless, there are several studies that show relatively small correlations between ASD-specific social deficits on the ADI-R, for example, and social adaptation reported in the Vineland Adaptive Behavior Scales (Kanne et al., 2011). Anderson et al. (2011) recently reported increases in the lethargy or social withdrawal scale from the Aberrant Behavior Checklist (Aman, Singh,

Stewart, & Field, 1985), a measure of behavioral difficulties in individuals with intellectual disabilities. The possibility is that, different social factors – such as social reciprocity/communication, social adaptation, and social withdrawal or perhaps motivation might provide clues into different dimensions of sociability and deficits.

Overall, research from both epidemiological studies (Rice, Schendel, Cunniff, & Doernberg, 2004) and from studies of the most commonly used diagnostic instruments, indicate that the social-communication dimension discriminates ASD from other disorders, but it has many limitations as a simple construct that can be meaningfully linked to neurobiological function (see for discussion: (Silverman, Yang, Lord, & Crawley, 2010). Recent empirical studies offer intriguing leads into important aspects of a social-communication dimension, but there is much more research to be done in this area.

Restricted, repetitive behaviors and interests as a dimension

Besides social-communication, the second dimension that is currently used to define ASD has to do with restricted, repetitive behaviors and interests (RRB). This is a very heterogeneous domain that includes stereotyped and repetitive behaviors, verbal and nonverbal; rituals and insistence on sameness; fixated or excessively circumscribed interests and unusual reactions to sensory input (see DSM-5.org). Large scale factor analyses of all items in comprehensive interviews and observation schedules such as the ADI-R (Lecavalier et al., 2006) and the ADOS (Gotham et al., 2007; R. Luyster et al., 2009) and of targeted RRB-related items in the same interview and observation schedule (S. L. Bishop, Richler, & Lord, 2006; Richler, Huerta, Bishop, & Lord, 2010) have all yielded a single factor that includes most of these subdomains. Many, though not all, of the specific examples listed in the proposed DSM-5 criteria and in the representations of DSM-IV criteria in the measures above are highly correlated with each other (see for example, Lord et al., 2000; Mirenda et al., 2010).

However, unlike the dimension of social reciprocity/interaction, analyses of RRBs from some of the major diagnostic instruments have also consistently yielded at least two, and sometimes three, separable subdomains or dimensions within the larger factor of RRB (Cuccaro et al., 2003).These separate dimensions have different trajectories across childhood and adolescence (Richler et al., 2010), different associations with intellectual disability (S. L. Bishop et al., 2006) and with language level (Kim & Lord, 2010; R. Luyster et al., 2009) and different patterns across gender (Hattier, Matson, Tureck, & Horovitz, 2011; Szatmari et al., 2012). The first subdomain, repetitive behaviors, including both motor stereotypies and use of objects (e.g., lining things up, flipping

things) and unusual responses to sensory input (e.g., peering out of the corner of the eye, smelling things) is very common in children and adults (Bishop et al., 2006) with ASD. Although they occur to some degree in the majority of children and adults with ASD (Bishop et al., 2006), these behaviors begin to decrease in intensity and in number in later school age years and adolescence, particularly in children without intellectual disabilities (Richler et al., 2010). These behaviors are also commonly observed in toddlers with ASD, but can be fleeting and may not be recognized as abnormal in small children (Robins, Fein, Barton, & Green, 2001; Wiggins & Robins, 2008) by parents or even clinicians, who may consider these behaviors relatively normal in children 2 years and younger (Leekam et al., 2007). However, even in toddlers, the number and intensity of these behaviors discriminates children with ASD from other children (Kim & Lord, 2010).

Second, behaviors related to rituals and insistence on sameness are somewhat less prevalent in ASD, occurring in approximately 25% of a sample of children with ASD under the age of 12 (S. L. Bishop et al., 2006). These behaviors tend to develop later in the preschool years and then to remain more stable over time, even in children without intellectual disability (Richler et al., 2010). Insistence on sameness has been put forward as a useful construct to be linked to neurobiology because it is less associated with age and language level/IQ than many other aspects of ASD (Hus, Pickles, Cook, Risi, & Lord, 2007).

A third subdomain has emerged with somewhat different characteristics across multiple studies. This is the dimension of circumscribed interests (Lam, Bodfish, & Piven, 2008; Tadevosyan-Leyfer et al., 2003), including highly fixated interests such as a particular Disney movie or weather, or very unusual preoccupations (e.g., shoe sizes, radiators, train schedules). In various analyses, items describing these behaviors have moved in and out of the two other subdomains described above, depending on the age of the participants (Bishop et al., 2006), but in a recent relatively large sample (Lam et al., 2008), a clear, separate factor emerged. This factor also plays a role within the Repetitive Behavior Scale-Revised (Bodfish, Symons, Parker, & Lewis, 2000).

A fourth kind of behavior often treated as an RRB is self-injurious behavior. These behaviors include biting the arm or hand, hitting or slapping the face and banging the head. Like repetitive behaviors, these actions are associated with intellectual disability, but unlike the more benign behaviors, when they occur with sufficient force to cause harm, they are much more rare (Dominick, Davis, Lainhart, Tager-Flusberg, & Folstein, 2007). Several recent analyses have suggested that their covariates and their course is different even from other repetitive motor mannerisms, such as hand flapping or banging objects, that may seem quite similar (S. L. Bishop et al., 2006; Esbensen, Seltzer, Lam, & Bodfish, 2009). They are frequently affected by environmental responses, but how they develop and, in some cases, what maintains them is not clear (Contrucci Kuhn & Triggs, 2009; King, 1993; Oliver, Hall, & Murphy, 2005). Self-injurious behaviors are not unique to autism, and so are not included in many diagnostic schemes, but are more common in ASD than in a general population.

RRBs are more heterogeneous and are often more context-dependent than social deficits. Yet the number and intensity of RRBs at age 2 was a unique contributor, besides IQ and social and communication deficits, to prediction of a stable autism diagnosis at ages 9 (Lord et al., 2006). Repetitive behaviors also contribute to parental stress, level of accommodations which parents are able to make (Carr & Lord, 2012) and academic achievement (Venter, Lord, & Schopler, 1992). Including RRBs in a diagnostic algorithm (Gotham et al., 2007) or in general screeners, such as the SRS, increases specificity considerably while changing sensitivity very little.

Relationship between social deficits and repetitive/restricted behaviors

Whether the social deficits that comprise ASD are always accompanied by RRBs is a source of debate among researchers and among clinicians. In a recent analysis of a multi-site genetics study for which the criteria were a diagnosis of any ASD, defined only in terms of social deficits and a communication deficit, only 9 out of over 2700 children failed to show repetitive behaviors either as reported by parents on a semi-structured interview or as observed by a clinician (Lord et al., 2012). In contrast, Walker et al. (2004), in a study of consecutive referrals to a clinic that specialized in children without intellectual disabilities found that over half of the individuals with PDD-NOS had no repetitive behaviors reported by parents on a questionnaire.

In part, the difference may lie in how the children were assessed. Unlike social behaviors, where parents or caregivers give straightforward answers to questions about specific social behaviors or contexts, often, when asked about one type of repetitive behavior, parents describe something quite different (Rutter, LeCouteur, & Lord, 2003). The ways in which RRBs are organized for DSM or ICD or in diagnostic instruments do not necessarily reflect either parental observations or the empirically developed factors. As with social deficits, more information about the nature of these behaviors and how they are affected by developmental and social contexts is much needed, particularly because they seem to offer an as yet untested glimpse into a behavior that may be less mediated by learning and

experience than are social deficits. The mystery as to why these behaviors are associated with social deficits continues, as longitudinal studies show that neither can social deficits account for RRBs nor do RRBs account for social deficits. Developmental changes in these dimensions follow different courses (Anderson, Oti, Lord, & Welch, 2009) and there is little evidence that deficits in one dimension cause the other, though interactions would not be surprising. Yet there are consistently high correlations in populations with ASD and related nonspectrum conditions between social-communication and RRBs [e.g., within modules of the ADOS, correlations range from 0.51 to 0.54 (Lord et al., 2000)].

What is also striking is that, as a dimension, particularly social reciprocity, but also RRBs, measured by any of the measures above, do not seem to be traits that are continuously distributed from typical development to autism. Neither are scores for measures that provide an overall total of items from both of these areas normally distributed (Gotham et al., 2007; Kim & Lord, 2012b). Most of the studies available are for children and either include a typical population with a small number of children with ASD (Constantino, Zhang, Frazier, Abbacchi, & Law, 2010), or a referral or at risk population with few or no typical children (Anderson et al., 2011). Recent studies with baby siblings of children with autism may help fill this gap (Elsabbagh et al., 2012; Ozonoff, Young, et al., 2011). However, in studies that used broader screening instruments with more typical populations (Scott, Baron-Cohen, Bolton, & Brayne, 2002; Virkud, Todd, Abbacchi, Zhang, & Constantino, 2009) and in studies of substantial numbers of children with ASD compared to controls matched on age and language level (Lord, Rutter, & Le Couteur, 1999) distributions of social deficits and of RRBs in ASD are quite distinct. Reports of one continuous distribution (Constantino & Todd, 2003) seem likely to be a function of two separate, overlapping distributions, a pattern that also seems likely to be relevant to measures such as the CAST (Scott et al., 2002), which has been frequently used in behavioral genetic studies. It is possible that the same is true for the Vineland (Kanne et al., 2011).

Does the lack of continuous distribution of social deficits and RRBs from typicality to ASD mean that there are not dimensions? In many ways, the lack of a continuous distribution of scoreis is not surprising, because items, at least for the standard ASD diagnostic instruments, were deliberately selected to discriminate ASD from other disorders and presumably from normal development (Rutter et al., 2003). Hyman (2010) argued that, with a dimensional threshold model, one might expect the greatest number of identified cases to score just right of a threshold (Helzer et al., 1985) which is quite different than what has been found for ASD, even in screeners intended for the general population. From a neurobiological point of view, this could mean that

what we are describing as social deficits or RRBs in ASD are simply not a valid 'human dimension' of behavior, but something patched together around messy conceptualizations of a categorical disorder. However, there also could be a different dimension, for example, a basic cognitive process, that has profound effects on social behavior AND repetitive behaviors and that would account for a more continuous distribution? (Dawson et al., 2005). Or the total scores could reflect multiplicative effects of dimensional social deficits and RRBs on each other that result in individuals, with ASD being, for the most part, set apart from others in many respects. This in turn comes back full circle to supporting the current proposal for a category of ASD determined by the dimensions but that may be more than the sum of its parts. Theories have been proffered, particularly in cognitive development, but there have been relatively few attempts to test directly refutable hypotheses about how these ideas apply to both dimensions (Frith & Happe, 1994). The point is that care has to be taken not to reify dimensions that may not be continuous but that may serve critical roles in quantifying and defining a larger category of ASD.

Other dimensions relevant to ASDs

Having an ASD does not protect a child or family from having other disorders, and in fact, increases the risk of a number of co-occurring behaviors and difficulties. These include hyperactivity and attention difficulties (Keehn, Lincoln, Muller, & Townsend, 2010; Yerys et al., 2009), and general behavior problems including disruptive behaviors and aggression, anxiety, depression and obsessive-compulsive disorder (Gjevik, Eldevik, Fjaeran-Granum, & Sponheim, 2011; Guttmann-Steinmetz, Gadow, & Devincent, 2009; Magnuson & Constantino, 2011; Mattila et al., 2010; Sukhodolsky et al., 2008). These issues are beyond the scope of this paper, but what is important in measuring and describing core features is that several recent studies have found that general behavior difficulties contribute to higher scores or 'lower specificity' for ASD screening measures, such as the SRS and the Children's Communication Checklist (Charman et al., 2007; Donno, Parker, Gilmour, & Skuse, 2010) in children with or without ASD.

Intellectual disabilities also co-occur with ASD very frequently, though the proportion of children with ASD who have IQs above 70 has increased dramatically (Rice, 2009; Croen, Grether, Hoogstrate, & Selvin, 2002). The relationship between IQ and symptom severity on almost every parent report measure of ASD is high (Berument, Rutter, Lord, Pickles, & Bailey, 1999; Hus et al., 2007). The exception is the SRS, where the relationship between total scores and IQ are more complicated (Constantino et al., 2007; Constantino, Przybeck, Friesen, & Todd, 2000). The ADOS has been able to

minimize the association between severity and current 'mental age' by recommending different modules and algorithms based on overlapping sets of behavioral items for children of different language levels (Lord et al., 2000). However, correlations with overall verbal IQ do remain, even with these provisions (Gotham et al., 2007). It is not surprising that children of different intellectual levels have different abilities to compensate for the deficits associated with autism, and that individuals with greater evidence of general difficulties in learning also have more specific difficulties in social-communication and a relative lack of flexible play and an increased amount of repetitive behavior. As for language level, comparisons of expected behavior in order to identify deficits specific to ASD must be made with regard to what is typical of an individual at that developmental level, age and intellectual ability. Recognizing intellectual disabilities is crucial in providing an adequate description of a child's behavior within the context of an autism spectrum disorder.

In addition, behaviors that are being considered as part of an NIMH effort to form neurobiologically based dimensional constructs may also be relevant, though not diagnostic of ASD (Insel & Cuthbert, 2009). These include executive functioning, fear and reward circuitry. While these dimensions are not the same as what is needed in clinical accounts of the distinctive behaviors of individuals with ASD, these neurobiologically based constructs may constitute important leads and insight into dimensions that impact quality of life in ASD and may offer avenues for treatment (Kraemer, 2008). A goal would be to more accurately represent the nature of social-communication deficits or specific repetitive/restrictive behaviors in the future to delineate similar dimensional constructs that might more specifically map onto core features of autism.

Other changes in diagnostic criteria

The proposed DSM-5 criteria offer a number of significant changes to the classification of ASDs, besides the shift from three to two domains. The proposed ICD-11 criteria are similar to DSM-5 in many ways; several points where the two systems agree and disagree, as of this writing, are identified below. Both new systems accept the term ASD, to replace pervasive developmental disorders (PDD). Today, there are few defenders of 'PDD' as nomenclature, though the original concept of expanding the concept of autism-related disorders beyond the relatively narrow conceptualization of Kanner's (1943) autism to include a broader group of individuals with language, play and social difficulties (Kanner, 1943; Wing & Gould, 1978) was a bold and clinically very important step. The notion of pervasive developmental disorders, introduced in DSM III-R (American Psychiatric Association, 1987) and then expanded to include PDD-NOS (not otherwise specified) in DSM

IV, was in response to this call for a shift in considering ASD as the convergence of these dimensional constructs.

One major change in DSM-5 is the formal acknowledgment that, at this point, a diagnosis of autism represents a name for a complicated set of behaviors believed to derive from yet unknown neurobiological causes and pathways. Arising out of this perspective is the proposal that there be a single category of behaviorally-defined ASD which encompasses all of the subtypes of Pervasive-Developmental Disorders, currently described in DSM-IV. Another criticism of existing diagnostic systems is the reliance on Not-Otherwise-Specified (NOS) diagnoses. This is particularly a problem in ASD, where several prevalence studies have found PDD-NOS to be more common than autism (Fombonne, 2003). Prevalence rates for the diagnosis of all ASDs increased 10-fold from 4 to 5 per 10,000 autism/up to a total of 10/10,000 of all ASDs in the 1990s to at or close to 1/100 currently for all ASDs (Croen et al., 2002; Rice, 2009). If we are to understand these increases in prevalence, it is critical to know if the increase is due to more milder cases or to increased numbers of all types of cases; with confusion about who has PDD-NOS versus who has autism or Asperger Syndrome, these patterns are difficult to discern (Bertrand et al., 2001). If atypical presentations of a disorder are more common than typical presentations, doubt is cast about the validity and usefulness of the categorical concept (Kraemer, 2008).

A recent multi-site study showed few consistent relationships between core features, but instead found marked site differences and effects of IQ, behavior problems and language level (Lord et al., 2012) in clinical diagnoses of Asperger Syndrome, PDD-NOS and autism in children with milder symptoms. In the new criteria, there is a single category of ASD. Distinctions between individuals with ASD and severe language deficit or no history of language delay or between individuals with ASD and average or greater intelligence from those with intellectual disabilities are made by specifying additional other diagnoses, such as communication and language disorders and intellectual disability or the lack of these diagnoses (e.g., ASD with high verbal and nonverbal intelligence). The new criteria eliminate the concern about the prevalence of NOS diagnoses and the confusion that surrounds the distinction between Asperger Syndrome, PDD-NOS and autism without intellectual disability or language delay by subsuming all ASDs within the umbrella category (Happe, 2011).Such an approach in the new systems should clarify the unreliable, highly varied approaches that clinicians currently use to differentiate milder cases of autism from Asperger Syndrome and PDD-NOS (Lord et al., 2012) and would avoid the current phenomenon of the same individual receiving serial or sometimes even

concurrent diagnoses of PDD-NOS, autism and Asperger Syndrome, depending on the knowledge and biases of their diagnostician (Klin et al., 2007; Miller & Ozonoff, 2000; Sharma, Woolfson, & Hunter, 2011).

In addition, rather than receiving different diagnoses, individuals who meet criteria for ASD who have a known genetic condition, such as Fragile X or Rett Syndrome, receive a standard diagnosis of ASD with these conditions designated as associated features of ASD (http://www.DSM5.org) or in ICD-11 with separate genetic conditions. This strategy also has the advantage of leaving room for new genetic and other biological findings that may shed light on etiology.

The two systems, DSM-5 and ICD-11, deal with boundaries just outside of ASD, in different ways. In ICD-11, the current proposal builds on genetic findings indicating that a broad range of behavior difficulties related to social-communication deficits, personality traits and restricted interests are more common in family members of individuals with ASD than in various comparison populations (Bolton, Pickles, Murphy, & Rutter, 1998; Pickles et al., 2000). DSM-5 takes a different approach, outlining a new disorder within the communication disorder category rather than within ASD. Referred to as social communication disorder, this category is intended to describe individuals who have significant social and communication difficulties similar to those in ASD, but without repetitive or restricted behaviors (http://www.DSM-5.org), rather than the full-range of 'boundary' conditions outside of ASD. How many individuals fall into this group is not clear. The social communication disorder as a category is similar to what D. Bishop described many years ago as semantic-pragmatic disorder (Bishop, 1989), with more explicit ruling out of children who meet the new ASD criteria. No data are yet available about its reliability, validity or prevalence. This is the area where there is the most disagreement and the least amount of useful data from standardized measures.

Rationale for developmental considerations

There are a number of important nosological issues related to development in ASD. ASD is a developmental disorder that is typically manifested in children in the second year of life (Ozonoff, Iosif, et al., 2011) and most often continues throughout the lifespan (D. K. Anderson et al., 2011). DSM IV and ICD-10 both included an age of onset criteria, which required a relatively nonspecific sign of difficulty within the domains that define ASD prior to 36 months (American Psychiatric Association, 1994; World Health Organization, 1992). However, the new criteria are broader indicating that behaviors associated with ASD must begin in early childhood but, for some children, may not be apparent until social

demands increase (http://www.DSM5.org). These changes in criteria reflect research on developmental differences and the need to incorporate such findings into diagnostic classification.

In part, the new approaches acknowledge that the age at which caregivers recognize that something is not quite right and the age at which professionals diagnose autism or a related condition are not the same as age of onset. Retrospective reports of dates are subject to complicated 'telescoping' which means that recollections are affected by the distance between the proposed event and the current date (Hus, Taylor, & Lord, 2011). Many recent studies of infant siblings (Ozonoff, Iosif, et al., 2011), studies of very-early referred toddlers (Lord, Luyster, Guthrie, & Pickles, 2012), and retrospective studies of videos (Werner, Dawson, Osterling, & Dinno, 2000) show that at least some children with ASD differ from other children by their first birthday. Not all children who develop ASD are identifiable as early, however. The variability in these findings across studies and across children, and longitudinal studies that have shown that a substantial proportion of children who develop ASD show slowing or loss of skills before 'onset', all suggest that the notion of 'regression' is more complicated than previously thought (Lord et al., 2012; Ozonoff, Iosif, et al., 2011).

Researchers have called for definitions of regression in terms of whether the child shows developmental delays or differences before a clear change, whether there is a gradual or more sudden shift in behaviors, when this happens and how many areas of development are affected, as part of specifiers in DSM-5. The reason behind omitting this group as a separate category in DSM-5 is that this pattern, while it clearly occurs, is extremely rare (Fombone, 2002), the behaviors that define childhood disintegrative disorders (CDD) after onset seem to fall well within the spectrum of autism (Volkmar & Rutter, 1995), and that they can be separately monitored through specifier codings for age and type of onset. In contrast, in the proposed ICD-11 criteria, children with marked, multi-system late onset (after age 2) regressions continue to be separately classified as having CDD. The logic behind the separate terminology is the need for different investigations and further very targeted research for this population (Volkmar & Rutter, 1995). Despite somewhat different nomenclatures, it should be possible to compare data for children falling within these groups across the diagnostic systems.

There is also a general concern about the need for criteria to address a wide range of behaviors within the context of very different developmental levels. This can range from toddlers, for whom families are seeking a first diagnosis, to primary school students with significant intellectual disabilities who have even more severe social-communication deficits and debilitating repetitive behaviors to label adults who

may have had many diagnoses in the past, but never a diagnosis of ASD. DSM-5 has elected to deal with the need for breadth by describing principles that define each subdomain (e.g., nonverbal/integration of verbal and nonverbal communication, social reciprocity, relationships and adjusting to social contexts) and then providing non-exhaustive examples that represent different ages and levels of development to represent these principles (http://www.dsm-5.org). This approach has created some confusion because, when attempts are made to match existing data from other frameworks onto the new criteria, many examples are simply not available (Mattila et al., 2011; McPartland, Reichow, & Volkmar, 2012). This has been interpreted to mean that individuals would no longer receive diagnoses of ASD, which is not the intention and should not be the case, if clinicians use the new DSM-5 criteria as intended.

Limitations of new diagnostic systems

One concern about the proposed new systems is the disenfranchisement of individuals with Asperger Syndrome (Baron-Cohen, 2009). Asperger Syndrome is often viewed by self-advocates and families as less stigmatizing and more descriptive of milder conditions of ASD than autism (for example see http://www.autism.org.uk). PDD-NOS is also generally considered less stigmatizing, but is such a source of confusion that there are few advocates for retaining the term. More importantly, the empirical data do not justify having separate categories for Asperger Syndrome or PDD-NOS, particularly when, in some states, individuals with these disorders are not eligible for autism services or benefits. The overall goal for the new criteria is to increase equity across the existing subcategories in terms of treatments covered by third party payers. There is no reason that advocacy organizations cannot continue to use the term Asperger or that people may not benefit from joining groups that define themselves in terms of previous definitions.

The new diagnostic frameworks in DSM-5 and ICD 11 are not yet finalized. To adequately test them, extensive field trials, including face to face assessments of large numbers of individuals across age and ability level who have and have not had previous diagnoses of ASD would need to be carried out, with systematic comparisons of diagnoses made using previous systems, including DSM-IV and ICD-10 by independent clinicians (presumably counter- balanced to use different frameworks at different times) (see Wing, Gould, & Gillberg, 2011). Ideally, this would occur for samples representative of different populations and across cultures, ethnic groups and races in different countries. The American Psychiatric Association has conducted field trials that include several thousand participants and clinicians at numerous sites in which clinicians were asked to

report whether patients met criteria for DSM-IV diagnoses and identify relevant DSM-5 diagnoses from a few targeted diagnoses for each sample. Unlike the DSM-IV field trials, these data are collected by clinics not supervised by committee members determining criteria. They consist of consecutive cases of both new referrals and existing cases, rather than recruitment of arbitrarily selected patients with current diagnoses. However, direct comparisons of criteria from the different systems were not made in the new trials, nor was the new Social Communication Disorders category tested. Such a set of field trials would be of value, but could be extremely expensive, especially for ICD-11 if inclusive of international populations. This leaves open highly politicized questions about whether the new sets of criteria will result in changes in prevalence rates (Carey, 2012; McPartland et al., 2012). Unfortunately, archival data sets, particularly brief questionnaires or registries, cannot adequately answer these questions because one of the major tenets of the DSM-5 criteria is to expand the examples possible with which to define each subdomain and the range of non-overlapping subdomains beyond DSM-IV and ICD-10; existing datasets are very unlikely to contain these examples unless they include very comprehensive, systematic assessments (see (Mandy, Charman, & Skuse, 2012).

Psychometric issues in developing classification measures

The major contribution of the DSM system was to focus on test-retest reliability of diagnoses (Kraemer, 2008). Reliability constrains everything else about a classification; reliability across raters, internal validity and construct validity (whether the diagnosis actually describes what is intended) are all limited by the extent to which the measure is consistent over time (assuming no marked change in the condition). Yet, as many have said, test-retest reliability is just the first step in having a useful classification system (Hyman, 2010). Although DSM can be criticized for this focus, the reality is that many existing and widely used measures of diagnostic features, at least in ASD, do not yet have particularly strong test-retest reliabilities across the most relevant age ranges (Lord et al., 1999; Scott et al., 2002). Thus, a continued goal for classifications must be reliability, extended from simple test-retest to include reliability across clinicians and other users. However, we cannot stop there, and attention does have to be paid to validity of diagnostic criteria, even though this is a cumbersome, complex process.

In fact, simple analyses of validity of screening measures have been limited by major methodological issues such as the blindness of diagnosticians to the purpose of the study (J. N. Constantino et al., 2003) and comparatively little serious investigation of specificity with appropriate clinical samples (Aldridge,

Gibbs, Schmidhofer, & Williams, 2012). However, concerns about validity are not limited to quick, easy to use screening measures, but also exist for more complex, difficult to administer diagnostic methods such as the ADOS and ADI-R (de Bildt et al., 2011). Although the two most commonly used research instruments have been reported as closely correlated (Kim & Lord, 2012a) (See Figure 3) when samples include both children with ASD and those with other disorders; with more restricted samples including only children with clear ASD, especially those of children with near-normal or normal intelligence, correlations between instruments are close to zero (D. Bishop, 2011). Analyses using various combinations of using the ADI-R and ADOS, indicate very poor specificity if one or the other measure, but not both, are positive (Risi et al., 2006) unless very high thresholds are set (Kim & Lord, 2012a). Both sensitivity and specificity are quite good when the instruments agree, but the notion of establishing continuous dimensions is limited by the minimal relationship between scores across instruments. Another promising approach to increasing specificity may be the use of convergent parent and teacher forms of the Social Responsiveness Scale (J.N. Constantino & Gruber, 2005); more data about this approach, including sensitivity will be helpful.

Researchers are eager to have severity scores that quantify social deficits according to interval scales because these scales can be linked to other quantitative measures (i.e. imaging (Coutanche, Thompson-Schill, & Schultz, 2011). However, the measures that have domain scores for social interaction and

repetitive/restricted behaviors, such as the ADI-R or the ADOS, do not provide this kind of score. Their total scores are additive and ranges are not based on true intervals. Severity scores proposed for the ADOS address this issue by tying severity to percentiles within populations of children with clinical diagnoses of nonspectrum, PDD-NOS/Asperger Syndrome and autism, but are still not true interval scales, particularly because most 'typical' children would be expected to score '0' or '1' (Gotham, Pickles, & Lord, 2009). Some researchers used counts of behaviors either as total scores (e.g., episodes of social acts, Drew, Baird, Taylor, Milne, Charman, 2007) or within particular items (see the Communication and Symbolic Behavior Scales (CSBS) (Wetherby & Prizant, 1993), but this is time-consuming to score and also often limited in the age ranges in which ASD can be discriminated. The importance of quantifying severity, beyond the previous categories of autism, PDD-NOS and Asperger, is that information is needed about individuals whose behaviors fall in the boundaries of the defined disorders.

In autism diagnoses, there have recently been some attempts to provide measurement tools that allow clinicians and researchers to take into account different considerations for discriminating inclusion or exclusion criteria. For example, alternative thresholds are provided for clinical diagnoses (where the assumption is that sensitivity, or accurate identification of all positive cases, is of higher priority) and research diagnoses (where accurate exclusion of false positive cases may be of higher priority) (Kim & Lord, 2012a; Lord et al., 2006). This follows the original model of ICD-10 where there were clinical diagnoses and more detailed research criteria (World Health Organization (Organization). However, even this distinction is not simple. If a treatment was highly invasive or had substantial risk, then one might propose that clinical thresholds be higher than research thresholds. In ASD, many of the more behavioral and developmental treatments might be expected to help even unaffected individuals, so that the conundrum may not be so much between risk of danger but between access to services and fear of stigmatization (Ruiz Calzada, Pistrang, & Mandy, 2012).

Within North America and Europe, questions of the effects of ethnic, cultural and socioeconomic diversity on diagnostic practices have been addressed, primarily in terms of prevalence rates and age of first diagnosis (Lord & Bishop, 2010; Shattuck et al., 2009). In the US, children of color and children whose parents are less well-educated are diagnosed later and are more likely to receive different diagnoses than ASD first than do other children (Mandell et al., 2009). Often research samples, even large ones (Fischbach & Lord, 2010; Gotham et al., 2008), have so few children of color or of less well-educated parents, that analyses of standard diagnostic instruments are minimal. However,
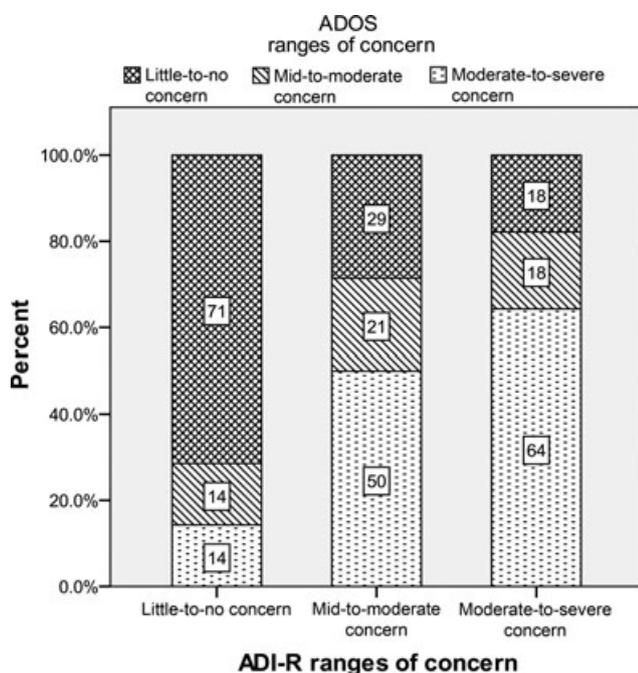

Figure 3 Illustration of convergence of ranges of concern for the toddler Autism Diagnostic Interview-Revised (ADOS) and Autism Diagnostic Interview-Revised (ADI-R) instruments. Reproduced from Kim and Lord (2012a), with permission

one longitudinal study that included substantial numbers of African American children as well as Caucasian children and of parents with a high school education or less showed no effects of race or of maternal education on either the ADI-R or ADOS throughout childhood. In contrast, Overton, Fielding, and de Alba (2008) in a small sample of Hispanic children had more inconsistent results and less specificity using the ADOS. Clearly, much more information about how diagnostic criteria are used and what defines different dimensions in children of diverse ethnic and socioeconomic backgrounds is needed.

In addition, studies of children and adults from non-English-speaking children and children from outside of western Europe are emerging. Many of the standard diagnostic instruments have now been translated into other languages; validation studies of children and adults in these countries will be very important, not just in order to ensure proper use of the measures, but also to determine differences in the ways in which the defining dimensions of social-communication and repetitive/restricted behaviors may be manifest in different cultures.

Conclusions

Ultimately, the first goal of a diagnosis must be clinical usefulness; nosology for the diagnosis of a disorder must address this aim (Kraemer, 2008). Categorical estimates of severity of ASD predict response to behavioral treatment (Sheinkopf & Siegel, 1998). Severity of dimensions within ASD such as social deficits and repetitive behaviors, predict outcome and stability of diagnosis (Lord et al., 2006). Research has begun to explore ways in which specific strengths (e.g., relatively good joint attention; interest in objects) or difficulties within core features or other dimensions (e.g., poor receptive language; high frequencies of repetitive behaviors) interact with different treatment approaches to result in better outcomes (Carter et al., 2011). At a time when neurobiological causes for ASD are diverse and non-specific, this clinical usefulness will not lie in links to etiology or even pathophysiology; it must be rooted in the provision of information that

advises selection of services that will increase independence and quality of life.

A diagnosis of ASD is also associated with other dimensions: increased risk for other behavioral difficulties, higher stress for families and less adequate healthcare (Lord & Bishop, 2010). Although there is overlap in both symptoms and needs for services between individuals with ASD and those with numerous other disorders, children, adults and families with a child with ASD often require more and different support and, families also report greater stress on average, than families with children with similar intellectual disabilities (Sanders & Morgan, 1997). Understanding how diagnoses, measurement of core dimensions in ASD and associated features affect response to treatment is extraordinarily challenging when interventions are broad, expensive and lengthy and cross boundaries among social systems including medicine, public health and education. The intertwining of social-communication and repetitive/restricted deficits in ASD and their interactions with other dimensions such as language level, intelligence and general behavioral difficulties, including anxiety, make the task of developing necessary and sufficient criteria even more complex. In addition, the power of a diagnosis to affect, both positively and negatively, the ways in which a person or a family conceptualizes behavior, cannot be underestimated (Ruiz Calzada et al., 2012).

In a recent presentation about the NICE Autism Assessment Guidelines for the National Health Service in the UK, Gillian Baird, the chair of the committee, outlined the results of the National Autism Society's survey of what parents and community pediatricians, the primary gatekeepers of diagnoses in early childhood, wanted from a diagnosis of ASD (Baird, 2012). As shown in Table 1, parents' priorities were to delineate the pathway that they should take through a health system pre and post diagnosis, provision of more support during and after a diagnosis and better awareness of co-existing conditions, along with decreased waiting times and improved interdisciplinary coordination. Pediatricians wanted stable, meaningful terminology, help in making differential diagnoses and reasonable

Table 1 Results of National Autism Society (UK) Survey for NICE Guidelines (adapted from Baird, 2012)

Parent concerns	Pediatrician concerns
A clear pathway for pre and postdiagnosis	Do not suggest a diagnostic process that is unworkable in an office context or that increases waiting times
Decreased waiting time and improved access to specialists	Clarify terminology to produce some consistency across professionals
Increased awareness of co-existing health problems and the uniqueness of each child's presentation	Give guidance for difficult differential diagnoses
Improve coordinated approach to diagnosis by different professionals	Clarify any biomedical investigations needed
Make diagnosis more collaborative with parents and improve support during and after diagnosis	

expectations for what diagnostic procedures entailed as well as clearer mandates for when biomedical assessments and interventions were needed. It is hoped that changes in the newly proposed diagnostic systems will address at least some of these issues, in terms of criteria that better help differentiate ASD from other disorders and better specification of co-existing conditions. However, other issues depend on efforts beyond the scope of diagnostic systems. Some of these issues would require disciplines to work together to achieve consensus on what constitutes a 'decision tree' of diagnostic procedures and differentiations that result in information that has direct bearing on selecting treatments and determining if progress is being made. Reliable, quantitative measures do exist for diagnosis and diagnostic dimensions, however, much could be done in terms of new instruments or improvements on existing ones to increase their usefulness in determining appropriate treatments and measuring treatment gains (see Dawson et al., 2010; Green et al., 2010).

What is next? Although often neurobiologists are impatient with the search for more accurate descriptions of behavior, we are far from understanding exactly what the behavioral deficits associated with ASD are, how they interact with strengths and how they are affected by opportunities (or lack of opportunities) for learning. The extensive developmental literature in autism has revealed many areas where primarily children, but sometimes adults, with autism differ from typically developing children or, in fewer cases, children with other disorders. We seem beyond the point of designing group studies which show that, on the average, children with autism have a mean difference on a certain measure compared to age-matched controls. Information about individual patterns and individual differences is critical, particularly if we are seeking links to neurobiology at an individual level. Fine-grained analyses of behavior patterns that are reliably manifest across time in at least some subsets of individuals with ASD and that are either independent or that interact in a predictable fashion with intelligence and language level still have much to offer. At the same time, more efficient clinical measures of severity, ideally within dimensions, are also needed, particularly for studying the boundaries of ASD.

Theories of why marked social-communicative deficits and repetitive, fixated behaviors co-occur in populations of ASD would help move the field to more accurately focus the continued search for neurobiological associations with behaviors. Neurobiological measures that do not require extensive averaging across individuals and that are replicable across time and laboratories are a critical future direction. Links with other disorders that share behavioral symptoms also offer important opportunities (Piven, Gayle, Landa, Wzorek, & Folstein, 1991), though it is critical that the shared symptoms truly overlap and do not just appear similar based because of similarly named questionnaires.

Although sometimes arguments occur around a choice between categories and dimensions, this is a false dichotomy. Dimensions can always be made into categories by defining thresholds and, as we see with the proposed DSM-5 and ICD-11 criteria, categories are formed from dimensions (Pickles & Angold, 2003). Rather, the question is for what purpose do we define and measure dimensions? To more accurately describe, predict and be able to change behavior? OR to link with neurobiological findings? If we move to conceptualizations of neurobiological pathways of development, rather than a disease that is present or not, then the role of dimensions changes. Behavioral dimensions would serve as the indicators of the need for different services and of response to treatments, as well as risk for associated problems. Behavioral dimensions would also become the indicators of how neurobiological changes occur, how they are intermeshed and how developmental pathways might be modified or built upon (Cicchetti et al., 2011; Rutter & Sroufe, 2000). This approach would involve reconsidering the meaning of the rich, complex findings from genetics and to some degree, from neuroscience, based on categorical conceptions of ASD and very broad dimensions. It would also require more attention to specificity of behaviors associated with ASD, and when non-specific dimensions are of interest, their interactions with core features.

For a behavioral disorder, ultimately what needs to be changed through treatment is behavior; neurobiological pathways are important because of their direct underlying association with behavior. In ASD, behaviors, such as highly repetitive actions, unusual reactions to the environment and aggression, and lack of behaviors such as basic nonverbal social communication, spontaneous functional language, more complex social understanding, independent self-care and engagement in age-appropriate activities, are sources of limitations and successes (D. K. Anderson et al., 2011; Pickett, Pullara, O'Grady, & Gordon, 2009), not just interesting links to neurobiology (Silverman et al., 2010).

In just the last 25 years, autism has gone from what was considered a rare, obscure, mysterious disorder that, for a long while, was attributed to poor parenting, to a common, frequently discussed heterogeneous neurobiological, but still mysterious condition that involves separate, critical dimensions of social-communication development and fixated, restricted behaviors and interests, and frequently co-occurring, but not universal, difficulties in language and general intellectual function (Fombonne, 2003). Many of the gains in awareness and research support have come from strong parent and community advocacy (http://www.Autismspeaks.org; http://www.autism-society.org; http://www.autism.org.uk).

As the awareness of ASD has grown, so has the media attention (Carey, 2012; Zarembo, 2011) and the speed with which news, accurate or not, spreads through the autism community. While it holds great promise, much neurobiological research has yet had little direct bearing on our understanding of what ASD is or how to treat it. Clinical research has improved the reliability and validity of diagnoses but with little attention to the trade-off between efficiency and sufficient documentation of individual differences in skills and needs ASD or the ramifications of diagnoses for appropriate treatments. Ideally, there would not have to be a choice between deriving information only with clinical utility OR linking with neurobiology. Nevertheless, at least within the scientific community, the latter is the over-riding priority (Regier, Narrow, Kuhl, & Kupfer, 2011). In contrast, as exemplified in the responses provided to the NICE committee, for the families and clinicians who work with individuals with ASD, the questions and priorities are quite different. The need for clear nosology and for balanced approaches that address immediate clinical concerns for individuals and families with ASD and neurobiological research that, in the long run, provides hope for new treatments has never been greater.

Acknowledgements

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Key points

- Autism spectrum disorders is a summary term for an as-yet-not-understood combination of social-communication deficits and repetitive/restricted behaviors and interests that interact together to form a pattern that appears to be more than the sum of its parts.
- Changes are being made to the DSM-5 and ICD-11 to reflect research suggesting that autism spectrum disorders (ASD) should be considered along dimensions of core features and additional crosscutting factors such as language delay and intelligence, rather than categories such as Asperger Syndrome and PDD-NOS.
- Finer-grained descriptions of behaviors associated with ASD are still needed in order to better define dimensions of social-communication deficits and restricted/repetitive behaviors on an individual level for both clinical and neurobiological purposes.
- Quantitative measures are needed that accurately map the different dimensions, independent of developmental factors such as age, language level and IQ and to address issues of boundaries of ASD.
- Quantitative measures are also needed that streamline information that is relevant to diagnostic dimensions are needed for clinical purposes; we need to understand how to use historical information along with clinician observation efficiently to maximize valid diagnoses and descriptions of dimensions.
- For the purposes of addressing the clinical needs of individuals with ASD and their families, we need to balance the requirements of clinical practice and the goals of neuroscience in nosological systems through more accurate descriptions, quantification of dimensions and interactions with other features, and analyses of individual patterns of behavior.

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