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Review

Autism spectrum disorders: An historical synthesis and a multidimensional assessment toward a tailored therapeutic program

Jean Xavier [a,*], Claude Bursztejn [b], Maitri Stiskin [c], Roberto Canitano [d], David Cohen [a,e]

[a] Department of Child and Adolescent Psychiatry, Université Pierre et Marie Curie, Assistance Publiques-Hôpitaux de Paris, GH Pitié-Salpétrière, Paris, France
[b] Department of Child and Adolescent Psychiatry, Université de Strasbourg, Strasbourg, France
[c] Department of Psychology, Brandeis University, Waltham, MA, USA
[d] Division of Child Neuropsychiatry, University Hospital of Siena, Italy
[e] Institut des Systèmes Intelligents et Robotiques (ISIR), CNRS UMR 7222, Université Pierre et Marie Curie, Paris, France

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ABSTRACT

Autism is a large group of disorders. From the first description in 1943 until know, attempts to propose nosological boundaries, through successive redefinitions of diagnostic criteria, have not succeeded in constraining the extensiveness nor in explaining the heterogeneity of autism. The failure of the categorical approach is revealed by several indices, including excessive comorbidity, the frequent use of Not Otherwise Specified categories and diagnostic uncertainty in borderline cases.

Several proposals have been formulated to categorize subgroups of children with complex severe developmental disorders but less severe trajectories than typical autism. The diversity and overlap in their clinical expression emphasize the importance of using a multidimensional assessment inscribed in a developmental perspective. In this way, clinicians could encompass the issues of the categorical approach, address the child holistically and then achieve a functional diagnosis enabling the elaboration of a tailored therapeutic proposal.

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* Corresponding author. Tel.: +33 142162342.
E-mail address: jean.xavier@psl.aphp.fr (J. Xavier).

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1. Introduction

Autism is a heterogeneous group of disorders, defined on purely behavioral grounds (Cohen, Volkmar, & Paul, 1986) and underlined by multiple etiological and pathophysiological substrates (Betancur, 2011; Cohen et al., 2005; Guinchat et al., 2012). This lifelong condition reveals a vast clinical variability in terms of expression and symptom severity, and in terms of neural deficits or associated medical conditions (e.g. seizures and intellectual disability, Amiet et al., 2013). Thus, "The autisms" present a clinical and therapeutic challenge as well as a challenge in research.

From the first description in 1943 until now, successive attempts to propose nosological boundaries have been marked by a dialectical tension between a categorical approach (CA) and a developmental approach through a multidimensional point of view. Successive redefinitions of diagnostic criteria have not succeeded in constraining the extensiveness nor in explaining the heterogeneity of autism. Following the medical tradition, the CA, which is used in the DSM, is based on cut-off points. It involves the inclusion or exclusion of a symptom or syndrome into a diagnostic category, as demonstrated by Kanner in his first description of infantile autism. Conversely, a developmental approach considers there to be continuity between normal and pathological features, measuring the intensity of an element of a behavior by locating its place on a continuum, each point of which is assigned a value. In 1965, Hempel criticized the inadequacies of the CA at portraying clinical reality, preferring instead a "multidimensional space" in which individuals are situated along different characteristics axes in a continuous distribution. Similarly, Eysenck (1964), dealing with a typology of personality, emphasized the utility of considering personality as a continuous phenomenon (e.g. dimensionally), rather than a discrete one (e.g. categorically).

The failure of the CA is revealed by several indices, including excessive comorbidity, diagnostic uncertainty in borderline cases, and the frequent use of NOS (Not Otherwise Specified) categories (Weintraub, 2011). Excessive comorbidity can be seen as a result of the DSM's focus on diagnostic accuracy (interrater reliability) rather than construct validity, thereby creating situations where the same patient can easily be classified under several comorbid diagnostic labels. Furthermore, as a consequence of strictly defined diagnostic categories, those patients who fall along the boundaries between diagnoses are considered to be borderline cases. These ambiguous cases, which are plentiful, contribute to the frequent use of NOS categories in which the clinician's opinion can take refuge when a suitable category cannot be found.

The somewhat arbitrary choice of categorical cutoff points is illustrated by debates between the lumpers and the splitters which reveal the need to strike a subtle balance between being too broad and being too narrow when determining diagnostic boundaries. In the field of autism, a more balanced approach was initiated by Wing and Gould (1979) who first proposed an autism spectrum disorder consisting of multiple axes. In the first section of this article, "Historical Perspectives," we will examine successive versions of the DSM and ICD, focusing on how they oscillate between the two approaches in an attempt to encompass the extensiveness and heterogeneity of autism. Then, to expand upon the points mentioned above concerning borderline cases and NOS categories, the second section of this paper will address the condition of PDDNOS, the most common diagnosis given to children on the autistic spectrum, yet a diagnosis which is not clearly clinically or psychopathologically individualized.

We will also discuss the issue of the categorization of PDDNOS children in the DSM-5, as well as the link between PDDNOS and other complex developmental disorders that share some of the same clinical features. The diversity of these disorders and the overlap in their clinical expression emphasize the importance of using a dimensional perspective. In the last section of this paper, we will highlight a multidimensional framework for addressing the Autism spectrum disorders in order to arrive at a functional diagnosis. By recognizing that no two cases of autism are the same and thus that one categorical diagnosis does not equal one "therapeutic package," this framework could provide a useful way to constrain the complexity and comorbidity in autism. This will allow us to make progress in research as well as to help clinicians offer their patients a treatment plan that is tailored to the individual.

2. Historical perspectives

2.1. Pioneers of autism

While Kanner (1968) was the first to clearly define the autistic disorder, the knowledge of this pathology is much older, as is evidenced by certain clinical descriptions. In the medical literature, Itard (Malson, 1964) was the first to describe a clinical picture suggestive of autism in his account of Victor, a child found on January 8, 1800 in the Aveyron region of France. The child was found mute and naked with an animal-like comportment, having lived in complete isolation from people and society. Pinel (1800), the founding figure of French psychiatry and the first physician to examine Victor, pronounced that

the boy was an "idiot," meaning that Victor was born with an incurable condition and was incapable of being educated. Itard, however, rejected Pinel's pessimistic prognosis, postulating instead that Victor's developmental problems were merely the result of his lack of contact with civilization. Itard proposed his own "moral treatment" of the wild boy, and engaged Victor in an educational program aimed at stimulating different senses through exercises of increasing complexity designed to promote thinking and language. This four-year intensive treatment, however, did not bring Victor to speak, nor to come out of the isolation in which he increasingly took refuge (Normand & Carrey, 1995).

In 1908, Heller described six cases of children who, after a period of normal physical and psychological development, began to deteriorate gradually or in spurts around the age of 3–4 years, resulting in a state of irreversible dementia after just a few months. In addition, the children exhibited unusual mannerisms and attitudes, as well as gestural and verbal stereotypies. Heller first named this disorder "*dementia infantalis*", and it was the first description of what would later be called "*childhood disintegrative disorder*". In 1943, Kanner described 11 children aged 2½–8 years who were unable to establish normal interpersonal relations, with an avoidance of eye contact, language troubles, stereotyped behavior, a need to maintain a stable and unchanging environment, and, sometimes, an astonishingly high memory capacity. These children with "Autistic Disturbances of Affective Contact" were described by Kanner as having two core symptoms: "extreme autistic aloneness" and an "anxiously obsessive desire for the maintenance of sameness." In 1944, Asperger coined the term "autistic psychopathy," depicting children who seemed to have high non-verbal intelligence quotients and who appropriately used a large vocabulary. This condition, now named Asperger Syndrome (AS), is characterized by marked social difficulties, particularly with peers, no significant delay in language or cognitive development, and a tendency to appear somewhat later in life than autism.

2.2. DSM and ICD era

In 1975, the Ninth Edition of ICD (International Classification of Diseases) gave official recognition to infantile autism. Previously labeled "*childhood schizophrenia*" in the earlier versions of the DSM, autism was first granted official recognition as a category in the DSM III introduced in 1980 (American Psychiatric Association [APA], 1980) and was grouped into a new class of conditions called pervasive developmental disorders (PDD) (Table 1). Criteria are organized into three key elements: (1) Severe and pervasive impairments in the development of social interactions, (2) communication, and (3) unusual interests and stereotyped patterns or behavior (RRB). According to the multiaxial classification introduced in the DSM-III, autism appears in Axis I (i.e. Clinical Disorders of Mental Illness) and its list of diagnostic criteria follows a monothetic format (the complete set of diagnostic criteria is necessary and sufficient for a diagnosis to be made). The definition of autism included in the DSM-III proved unsatisfactory in several aspects (Volkmar, Bregman, Cohen, & Cicchetti, 1988): criteria were mostly applicable to younger and more impaired individuals, and they did not sufficiently encompass issues of developmental change (Cohen et al., 1986).

To address these issues, the criteria in DSM-III-R (APA, 1987) were judged with regard to the individual's intellectual level (Waterhouse, Wing, Spitzer, & Siegel, 1992) in an attempt to encompass the entire spectrum of the syndrome throughout different developmental stages and across the life span. A new term, PDD Not Otherwise Specified (PDDNOS), was introduced to describe children with some autistic features, but not the full criteria needed for a diagnosis of autism (Table 1). The DSM-III-R included a polythetic definition (all criteria were given equal weight, and a threshold was set for the number of criteria required in order to make a diagnosis). Registered in Axis 2 (i.e. Personality Disorders and Mental Retardation), PDD became a developmental disorder. The DSM III-R broadened the diagnostic concept (Volkmar et al., 1988) and compared to the DSM-III, had greater sensitivity but less specificity (Volkmar et al., 1988). A major issue for the DSM-IV (1994) and then for the DSM IV-TR (Table 1) was to balance the sensitivity and specificity of the diagnostic approach.

The DSM-IV criteria were designed to be consistent with the multiaxial system of the ICD-10, which appeared in 1993 (Table 1) and included the category of "atypical autism" to address cases where criteria are met in one or two but not all three of the areas required, or where all 3 criteria for childhood autism are met but appear at an age greater than 3 years. The 1994 version of the DSM IV (Table 1) allowed a PDDNOS diagnosis to be given to anyone with significant impairment in any one of the three domains. In the revised version of the DSM IV (2000), PDDNOS became a more restrictive category; impairment in two domains was required, one of which had to be the social domain. The DSM-IV uses a polythetic definition for the autism spectrum disorders and includes several additional subtypes within the PDDs, including Asperger syndrome (AS). This diagnosis was subject to a high degree of unreliability amongst expert clinicians, especially in regard to its differentiation from autism without intellectual disability (so-called "high-functioning" autism (HFA)) (Kamp-Becker et al., 2010, and for a systematic review see Witwer & Lecavalier, 2008).

The PDDs constitute a public health problem with a prevalence that has increased greatly over the years (median of 17/10,000 for AD and 62/10,000 for all PDDs) [Elsabbagh et al., 2012]. Several explanations, ranging from certain to more questionable, underlie this steady increase (for more details see Matson & Kozlowski, 2011): the use of new assessment instruments, a trend toward better identification and earlier recognition (Posserud, Lundervold, Lie, & Gillberg, 2010), constant changes in and expansion of diagnostic criteria over time (Fombonne, 2005; Rapin, 2002), inaccurate diagnoses (Barbaresi, Colligan, Weaver, & Katusic, 2009; Leonard et al., 2010), and social pressure to move many cases from intellectual disabilities (ID) to ASD (Weintraub, 2011). Because the DSM-IV's system of classifying autism cases into separate and discrete subtypes demonstrated limited reliability (Mayes et al., 2014; Rutter, 1978), the DSM-5, introduced in May 2013, officially replaced PDD [DSM-IV-TR] (American Psychiatric Association, 1994, 2000) with Autism Spectrum Disorder (ASD), a term which was already commonly used in clinical practice.

Table 1
Successive versions of Autism in DSM and ICD.

ICD-9 (1975)	Psychosis with origin specific to childhood	Infantile Autism Disintegrative psychosis (=Heller's syndrome) Other (=atypical childhood psychosis) Unspecified (=child psychosis NOS, childhood schizophrenia NOS)
DSM III (1980)	PDD	Infantile autism (before 30 months) Childhood onset pervasive developmental disorder (30 months–12 years). Atypical pervasive developmental disorder (onset not specified).
DSM III-R (1987)	PDD	AD (onset during infancy or childhood) PDDNOS (onset not specified).
ICD-10 (1993)	PDD	Childhood autism Atypical autism Rett's syndrome Other childhood disintegrative disorder Overactive disorder associated with mental retardation and stereotyped movements Asperger's syndrome Other PDD PDD unspecified
DSM IV (1994) and DSM IV TR (2000)	PDD	AD Asperger's Disorder. Rett's Disorder. Childhood Disintegrative Disorder. PDD-NOS
DSM-5 (2013)		ASD Social (pragmatic) Communication Disorder

ICD: International Classification of Diseases (WHO); DSM: Diagnostic and Statistical Manual of Mental. Disorders (APA); AD: autistic disorder; PDD: pervasive developmental disorders; NOS: not otherwise specified.

ASD is a single diagnostic category encompassing Autistic disorder (AD), Asperger Disorder (AS), Childhood disintegrative disorder, and pervasive developmental disorder not otherwise specified (PDDNOS). The categorical approach in the DSM-5 is complemented by a dimensional aspect involving (1) a system for quantifying inter-individual variations in severity; and (2) certain specifiers, such as association with other disorders, level of verbal achievement, and cognitive abilities. In addition, the three symptom domains of PDDs have been reduced to two [social-communication and restrictive, repetitive patterns of behavior (RRB)] in the DSM-5. Unusual sensory responses were added within the RRB domain reflecting the prevalence of this behavior in ASD (Ben-Sasson et al., 2009; Wiggins, Robins, Bakeman, & Adamson, 2009). The DSM-5 combines a monothetic format for social communication symptoms with a polythetic format for RRB.

2.3. Comparison of DSM-IV and DSM-5: first empirical studies

A number of studies have compared the DSM-5 and DSM IV-TR classification systems. A retrospective study found few differences between them in terms of sensitivity but demonstrated an improved specificity of the DSM-5 criteria for AS and PDD-NOS (Huerta, 2012). However, the majority of studies agree that the DSM-5 allows for better specificity but that this advantage comes at the expense of reduced sensitivity, and that children excluded by the DSM-5 are mostly those without intellectual disabilities who had fit into the PDDNOS category in the DSM-IV classification (Gibbs, Aldridge, Chandler, Witzlsperger, & Smith, 2012; Matson, Kozlowski, Hattier, Horovitz, & Sipes, 2012; Mayes, Black, & Tierney, 2013; Mcpartland, Reichow, & Volkmar, 2012; Young & Rodi, 2014). Confirming these results, Mayes et al. (2014) found that the most common reason for exclusion was a failure to satisfy all three criteria within the non-verbal social-communication domain.

This may have important consequences in countries that do not have free access to care and that require patients to have a positive diagnosis in order to access social/educational support services. To address this issue, "Social (Pragmatic) Communication Disorder" (SCD) has been added as a new category outside of ASD in order to provide labeled diagnostic coverage to children who exhibit milder social communication problems without repetitive or stereotyped behaviors. It constitutes a diagnostic home for some PDDNOS cases and also for children with significant pragmatic language disorders and co-occurring social delays (Ozonoff, 2012; Volkmar & Reichow, 2013).

According to the DSM-IV-TR diagnostic criteria, PDDNOS represented the majority of PDD cases, occurring at an average estimated prevalence of 37.1/1000, with Asperger syndrome and disintegrative disorder diagnoses being relatively scarcer (Fombonne, 2009). However, even though PDDNOS is such a frequent diagnosis, it is characterized by lack of a real conceptual and nosological framework; it is a subthresold category defined by "what it is not autism" (Tidmarsh & Volkmar, 2003; Towbin, Pradella, Gorrindo, Pine, & Leibenluft, 2005). The fact that PDDNOS is much less studied and has not been clearly clinically or psychopathologically individualized can at least in part be explained by the polymorphism of its clinical expression. The behavioral sameness observed in autism is replaced in PDDNOS by great symptomatic variability between different children or even for the same child at different developmental stages, which contributes to poor interrater reliability. There have been fewer studies performed to examine the predictive validity and stability of this diagnostic category. Matson and Boisjoli (2007) indicated that the developmental trajectory of these children is marked by

heterogeneity and that this diagnostic category is much less stable over time than autism. These results were confirmed in a meta-analysis by Rondeau et al. (2011), who demonstrated that the diagnostic stability of AD is significantly (around two-fold) higher than that of PDD-NOS. These results are consistent with the findings of the recent systematic review by Woolfenden, Sarkozy, Ridley, and Williams (2012), which included 23 studies from 1989 to 2006 that assessed the diagnostic stability of ASD. In this study, AD appeared to be a stable diagnosis, with a stability estimate of 89% at the highest; only a minority of children, around 12–15%, particularly those diagnosed in the preschool years with cognitive impairment, will no longer meet diagnostic criteria for any ASD after a period of follow-up. For other forms of ASD (i.e., PDD–NOS and AS), the study showed a lack of stability, with a highly variable pattern of stability between different reports, ranging from 14% to 61%. The qualitative study trajectories also indicated that PDD-NOS represents a heterogeneous group that includes prodromic expressions of later or less severe forms of AD (Stone et al., 1999), presentations corresponding to improvement of an initial typical autistic syndrome (Leroy et al., 2010), and disorders involving developmental delays in interaction and communication difficulties (Buitelaar & Gaag, 1998).

Recently, for a large cohort of children (7–12 years of age) in Seoul Korea, Kim et al. (2014) computed the prevalence of DSM-5 ASD and social communication disorder among children meeting diagnostic criteria for DSM IV PDD. They found that 71% of individuals with a DSM IV PDD-NOS diagnosis have DSM-5 ASD. Most of the remaining 29% correspond to individuals who have milder ASD symptoms, average intelligence, and less functional impairment, meeting the criteria for SCD. They concluded that the combined prevalence of DSM-5 ASD + SCD seems to be identical to that of every DSM-IV PDD category. Taking into account the PDDNOS category and particularly its link with other complex developmental disorders that share some of the same clinical features, we are led to question the limitations of a categorical perspective. Effectively, when children with some symptoms of PDD are referred to psychiatric clinics for difficulties in school integration and for behavioral and learning disorders, they might receive, in addition to PDDNOS, several comorbid diagnoses, which we will discuss in the next section.

3. Children with complex developmental disorders: the limits of a categorical approach

Several proposals have been formulated to categorize subgroups of children with complex severe developmental disorders but often less severe trajectories than typical autism. These disorders include multiple domains of dysfunction and impaired development. The diversity and overlap in their clinical expression emphasize the importance of using a multidimensional perspective in particular for clinical assessment.

3.1. Multiple complex developmental disorder (MCDD)

Cohen et al. (1986) proposed the term Multiplex Developmental Disorder (MDD) to identify, within the PDDNOS category, a heterogeneous group of children with atypical development (Dahl, Cohen, & Provence, 1986), including early-onset emotional and behavioral problems. This population has been given different diagnostic labels, such as "borderline children" (Bemporad, Smith, Hanson, & Cicchetti, 1982; Pine, 1974) or "schizotypal children" (Nagy & Szatmari, 1986). Their multiple and complex disturbances bordering on the autism category could be, according to the DSM-III (American Psychiatric Association, 1980), included in "Childhood-Onset Pervasive Developmental Disorder" (see above). In contrast to children with autism, they tend to have more optimistic outcomes and a later age of onset of symptoms (from 3 or 4 years). These children show marked instability, as well as variability and unpredictability in their social abilities; although they can at times exhibit normal social relations, at other times they can display inappropriate anxious responses, disruptive behavior and over-involvement with fantasy figures blurring their reality testing. A dysfunction in the dynamic process of self-construction underlies their impairments in social adjustment, school performance, and emotional lability (Paul, Cohen, Klin, & Volkmar, 1999).

MDD has been operationally defined according to criteria in three domains (emotional, cognitive, and social) in which disturbances are observed (see Box 1). Towbin, Dykens, Pearson, and Cohen (1993) changed the term MDD to multiple complex developmental disorder (MCDD) and validated this construct. Van Der Gaag, Buitelaar, Van Den Ban, Bezemer, and Van Engel& (1995) showed a clear differentiation between MCDD and autism captured by the criterion "fluctuations in the level of functioning". Later, they succeeded in validating a criteria-scoring algorithm for MCDD (Buitelaar & Gaag, 1998). Comparing neuropsychological profiles of three groups of children [MCDD, attention-deficit/hyperactivity disorder (ADHD) and controls], Lincoln, Bloom, Katz, and Boksenbaum (1998) found that the MCDD group displayed significant impairments in the areas of executive control and motor planning which corresponds to the diagnosis of developmental coordination disorders in the DSM-5 (for more details see Ad-Dab'bagh & Greenfield, 2001). Children with DCD are less involved and engaged in play (Green et al., 2011; Smyth & Anderson, 2000) and are more socially isolated than their typically developing peers (Cummins, Piek, & Dyck, 2005; Kennedy-Behr, Rodger, & Mickan, 2013). They also face emotional difficulties (Green, Baird, & Sugden, 2006; Xavier, Tilmont, & Bonnot, 2013) related to internalizing problems (Dewey, Kaplan, Crawford, & Wilson, 2002), such as depression, unfounded fears and phobias, or excessive worries.

3.2. Developmental disharmony: a developmental and dimensional approach

The term "Developmental Disharmony" was originally proposed in 1965 by Anna Freud to describe the "uneven progression rate in drive and ego development" which can lead to serious pathological consequences. This notion is linked to

Box 1. Diagnostic criteria for MCDD (reproduced from Cohen, Towbin, Mayes, & Volkmar, 1994)

1. **Regulation of affective state and anxiety is impaired beyond that seen in children of comparable age, as exemplified by at least two of the following**:

   1. 1.intense generalized anxiety or tension
2. fears and phobias (often unusual or peculiar)
3. 3.recurrent panic episodes or 'flooding' with anxiety
4. episodes of behavioral disorganization punctuated by markedly immature, primitive, or violent behaviors
5. significant and wide emotional variability with or without environmental precipitants
6. frequent idiosyncratic or bizarre anxiety reactions

2. **Consistently impaired social behavior/sensitivity, as exemplified by at least two of the following**:

   1. social disinterest, detachment, avoidance, or withdrawal despite evident competence
2. severely impaired peer relationships
3. markedly disturbed attachments; high degrees of ambivalence to adults (esp. parents/caretakers)
4. profound limitations in the capacity for empathy or understanding others' affects accurately

3. **Impaired cognitive processing (thinking disorder) beyond that seen in children of comparable age, as exemplified by at least two of the following**:

   1. irrationality, sudden intrusions on normal thought process, magical thinking, neologisms or repetition of nonsense words, desultory thinking, blatantly illogical, bizarre ideas
2. confusion between reality and inner fantasy life
3. 3.perplexity and easy confusability (trouble understanding social processes or keeping thoughts 'straight')
4. delusions, overvalued ideas including fantasies of omnipotence, paranoid preoccupations, overengagement with fantasy figures, grandiose fantasies of special powers, and referential ideation
5. The child is not suffering from autism
6. Duration of symptoms for at least 6 months

that of "developmental lines" by which Anna Freud intended to describe the progressive evolution of psychic functions from their earliest origins to their mature, adult forms. Some years later, this concept has been introduced in psychopathology. The notion of Disharmony focuses on the idea of a "maturative heterochrony" (Zazzo, 1964) in child development considered to be an interconnection between different dimensions (language, motor, cognition, affectivity). This functional shift can appear between and/or within each dimension.

This cluster of symptoms can be found within the limits of the categories defined in classification systems with multiple comorbidities (e.g. Autistic disorders and ADHD). Depending on which dimension was highlighted most, two labels were proposed: 'Developmental Psychotic Disharmony' (Misès et al., 1988) with an emphasis on emotional regulation and construction of the self, and 'Cognitive Disharmony' (Gibello, 1976) with an emphasis on cognition. In 1997, Tordjman et al. organized a working group of experts to compare French and American concepts of MDD and Disharmony (Dis), identifying a set of operationalized diagnostic criteria for each of the two constructs highlighting the similarity and the differences between the two concepts. Xavier et al. (2011) confirmed the reliability, the diagnostic efficiency and the validity of the disharmony construct (Dis) and explored the concordance between Dis, MCDD and ASD. They found a significant concordance between Dis and ASD, but no concordance between Dis and ASD subtypes (AD or PDD-NOS). Furthermore, disharmony seems to be similar to the notion of MCDD with a significant diagnosis concordance between the two constructs.

To explore some developmental lines, we conducted three studies in children with PDDNOS, each participant fulfilling criteria for Disharmony and MCDD. The first study dealt with the emotional dimension described in the two concepts. The study revealed great heterogeneity within our PDD-NOS sample with regard to their neutral, emotional and multimodal skills; this finding questions the internal validity of this diagnosis. Compared to typically developing children, the PDD-NOS group efficiently processed auditory, visual and multimodal stimuli on neutral tasks, but performed significantly worse on emotional tasks, particularly those with angry and neutral faces (Vannetzel, Chaby, Cautru, Cohen, & Plaza, 2011). In a second study we explored language profiles in four groups: children with autism, with PDD-NOS/Dis/MCDD, with specific language impairments (SLI) and typically developing controls. We found that language skills in autism and SLI rely on different mechanisms, while children with PDD-NOS/Dis/MCDD show an intermediate profile sharing some characteristics of both the Autistic and SLI groups. Our study suggests that expressive syntax, pragmatic skills and some intonation features could be considered as language differential markers of pathology (Demouy et al., 2011). The third study evaluated prosody using an automatic system to assess children's grammatical prosodic skills. Autistic and SLI children hardly expressed their emotions through prosody, but disharmonic children were able to do so and even seemed hyper-emotional compared to normal children (Ringeval et al., 2011).

Box 2. Multi-dimensional impairment (McKenna et al., 1994)

1. Poor ability to distinguish fantasy from reality, as evidenced by ideas of reference and brief perceptual disturbances during stressful periods or while falling asleep.
2. Nearly daily periods of emotional lability disproportionate to precipitants.
3. Impaired interpersonal skills, despite desire to initiate social interactions with peers.
4. Cognitive deficits associated with childhood-onset schizophrenia or attention-deficit hyperactivity disorder (ADHD).
5. Absence of thought disorder.

ADHD: attention deficit/hyperactivity disorder.

Box 3. Diagnostic criteria for DAMP (Gillberg, 2003)

(1) ADHD as defined in the DSM-IV
(2) DCD as defined in the DSM-IVCondition not better accounted for by cerebral palsy
(3) Not associated with severe learning disability – that is, IQ should be higher than about 50
(4) Other diagnostic categories often apply (for example, autism spectrum disorder, ODD)

ADHD: attention deficit/hyperactivity disorder; DCD: developmental coordination disorder; ODD, oppositional defiant disorder.

3.3. Multi-dimensional impairment

Similar to MCDD, other PDD-like symptoms were described in a clinical and neurobiological study led by the National Institute of Mental Health involving children with very early onset schizophrenia (onset of psychotic symptoms before age 12). One third of the children with psychotic disorders not otherwise specified were labeled multi-dimensionally impaired (MDI). MDI children exhibit some of the clinical features seen in ASD (Kumra et al., 1998). Under stress, they have intermittent episodes of hallucinations and delusions, affective instability, and complex developmental impairments. In addition, they appear eager for relationships but are socially deficient and experience severe emotional disturbances, affective instability and impulsivity (see Box 2).

This symptomatology suggests some DSM diagnosis, without meeting full criteria for PDDNOS, Asperger syndrome, bipolar disorder, intermittent explosive disorder, borderline personality disorder or schizotypal personality disorder. Children with MDI have neuropsychological deficits such as receptive/expressive language disorders, memory impairments and visuo-spatial difficulties (McKenna et al., 1994). Kumra et al. (2000) conducted a comparative study examining children with MDI and children with childhood-onset schizophrenia according to neuropsychological evaluations including (1) visual motor processing/attention, (2) abstraction-flexibility, (3) verbal intelligence/language, (4) spatial organization, (5) and memory and learning (verbal and visual). The majority of patients in both groups were found to have a similar pattern (in type and severity) of cognitive deficits for all six of these domains of cognitive functioning with the exception of two subtests: for the coding and digit symbol subtest and digit span subtest in (1), the MDI group was more impaired, and for memory and verbal learning in (5), the opposite result was found. McKenna et al. (1994) conducted an in-person screening of 71 subjects (children and adolescents) with an onset of psychosis at or before age 12 years. Among these patients, they found that the children in the MDI group had higher rates of ADHD comorbidity (85% vs 35%) and were referred more frequently and at an earlier age for behavioral and language problems.

3.4. The deficit in attention, motor control and perception (DAMP)

The concept of deficits in attention, motor control and perception (DAMP) was proposed by Gillberg (2003) and is defined by the combination of ADHD and developmental coordination disorder (DCD) (see Box 3). Gillberg stressed the high rates of overlap observed for these two disorders but insisted that the DAMP construct does not correspond to a simple addition of ADHD and DCD criteria, but rather to their interaction during child development. This condition has several comorbidities within other diagnostic categories, such as major depression or Oppositional defiant disorder. Furthermore, in severe cases of DAMP, autistic features are extremely common, with some cases meeting full operationalized criteria for Asperger syndrome. The high frequency of comorbidity also involves learning problems (e.g. in reading or writing and in mathematics abilities), as well as speech and language disorders.

4. A trial to encompass heterogeneity: toward a developmental approach

Successive redefinitions of autism diagnostic criteria have neither succeeded in constraining the extensiveness nor in explaining the heterogeneity of autism. On the contrary, there has been an increase in prevalence and subsequently an

increase in heterogeneity, a trend that is even more acute in the context of PDDNOS, a diagnosis that shares some clinical features with several complex developmental disorders. Over the years, the still relevant issue of "where to set its boundaries" has led to (1) successive modifications and subsequent expansion of diagnostic criteria, (2) the use of a monothetic or polythetic format or their combination in DSM-5, and (3) the oscillation of ASD's place between clinical axis 1 (in DSM III and IV) and developmental axis 2 (in DSM-III-R). The frequency of comorbid disorders is a complex issue given that comorbidity is the core component of autism heterogeneity, especially when the five other neurodevelopmental disorders mentioned in the DSM-5 are involved (Waterhouse et al., 1992). Despite the existence of specifiers, ASD criteria do not capture the variability and complexity of the disorder in research.

Integrating both a categorical and a multidimensional point of view in order to provide a more fine-grained taxonomy, Lai, Lombardo, Chakrabarti, and Baron-Cohen (2013) suggest expanding the list of specifiers to include developmental patterns, gender, non-ASD clinical specifiers (co-occurring conditions, motor disabilities, etc.), and cognitive profiles (intelligence, language skills, social cognition, executive functioning, etc.), as well as genetics and environmental risks. Similarly, Grzadzinski, Huerta, and Lord (2013), describes several dimensions that researchers should consider "beyond the variability in the presentation of core symptoms of ASD" when characterizing their ASD subjects in order to identify possible subtypes. Their non-exhaustive list includes cognitive and adaptive functioning profiles, language skills, patterns of onset, comorbid symptoms (ADHD, mood disorders, etc.), other medical conditions, and concerning behaviors. In order to improve the specificity of the diagnostic criteria, it is surely necessary to increase the list of specifiers, taking into account non-ASD-specific characteristics and other behavioral dimensions.

But one question remains: when will this list be exhaustive enough to respond fittingly to the complexity of the clinical reality? We know that this distinction between ASD core symptoms and non-ASD symptoms (i.e. associated features) is useful for the sake of conceptual clarity. But, is it clearly applicable in clinical practice when faced with an individual patient? Several studies have shown a high frequency in ASD of Intellectual Deficit ~55–70% (Amiet et al., 2008; Charman, 2011), of Attention Deficit/Hyperactivity Disorder ~30% (Ronald & Hoekstra, 2011), and of Motor Disorder ~70% (Downey & Rapport, 2012). Concerning language deficits, clinical presentations of ASD patients differ in light of their level of structural language impairment (Luyster, Kadlec, Carter, & Tager-Flusberg, 2008). Certain researchers have found similarities between the impairments of individuals with SLI and ASD, as well as an overlap in their social and communicative deficits (Bishop, 2003; Leyfer, Tager-Flusberg, Dowd, Bruce Tomblin, & Folstein, 2008) although development of linguistic structure appears more pervasive in ASD than in SLI (Demouy et al., 2011).

The multidimensional approach cannot only be defined as being statistically related to a categorical approach by defining a threshold. This is only valid when two assumptions are verified: (1) the distribution should be a normal one, which is not always the case for autism when examined at the level of major risks factors. E.g. in the case of Tuberous Sclerosis, it has been shown despite common genetic causal involvement that clinical phenotype was bimodal: on one hand a severe phenotype including ID, ASD and epileptic encephalopathies; on another hand, a mild phenotype with normal or borderline intelligence and ASD (Ouss et al., 2014). (2) The targeted impairment must not impact other dimensions, meaning that modularity in cognitive development is always verified. This is not the case in ASD, as it has been shown by developmental studies. For language, Demouy et al. (2011) have shown that modularity and correlation with age was verified for the language dimension (lexicon, syntax, semantic and pragmatic) in SLI. On the contrary no correlation between language dimension and age was found in ASD.

Because "Varied genetic and varied environmental risk factors have suggested that autism is many different disorders under one name" (Waterhouse, 2013), the single behavioral diagnosis of ASD does not by itself offer the keys to a tailored therapeutic strategy. The diversity of complex phenotypes corresponding to ASD which explains the excessive comorbidity associated with this disorder and emphasizes the inaccuracy of DSM, is confirmed at an etiological and pathophysiological level. Genetic factors with many gene variants that seem to affect brain development and synaptic functions have been reported in association with ASD (Amiet et al., 2013; Betancur, 2011; Han, Tai, Jones, Scheuer, & Catterall, 2014). However current research findings contradicted one individualized theory of pathophysiology in autism (Nesse & Stein, 2012; Silver & Rapin, 2012; Vissers, Cohen, & Geurts, 2012). Moreover, taking into account comorbidities mentioned above, ASD and ADHD seem to be underlined by common neurobiological dysfunction (Gargaro, Rinehart, Bradshaw, Tonge, & Sheppard, 2011; Rommelse, Franke, Geurts, Hartman, & Buitelaar, 2010). Several studies support the notion that ID and autism share a common molecular etiology with the same genetic variants found in both disorders (Nishiyama et al., 2009; Van Bokhoven, 2011; Wall et al., 2009).

Should not the associated features be seen as contributing factors in a child's development that influence the very expression of the core autistic symptoms? Consideration of the existence of these comorbid factors form the basis for the label of more homogenous and clinically meaningful subgroups within ASD, and the identification of biomarkers leading to delimit subgroups with unique etiologies or risk factors. This process has, for individuals with ASD, tremendous implications in terms of vulnerability to other disorders, prognosis, and the design of a therapeutical project including novel treatment targets. In reviewing several classification proposals in Section 3, our purpose is not to solve the problems posed by the categorical approach by offering alternative diagnosis that could replace current diagnosis in the DSM. We would rather emphasize the complexity and diversity of clinical situations corresponding to the "NOS" existing categories. In Fig. 1, we attempt to describe these complex developmental disorders by addressing each of them through several specific dimensions, which are integrated in the multidimensional assessment described in Table 2.

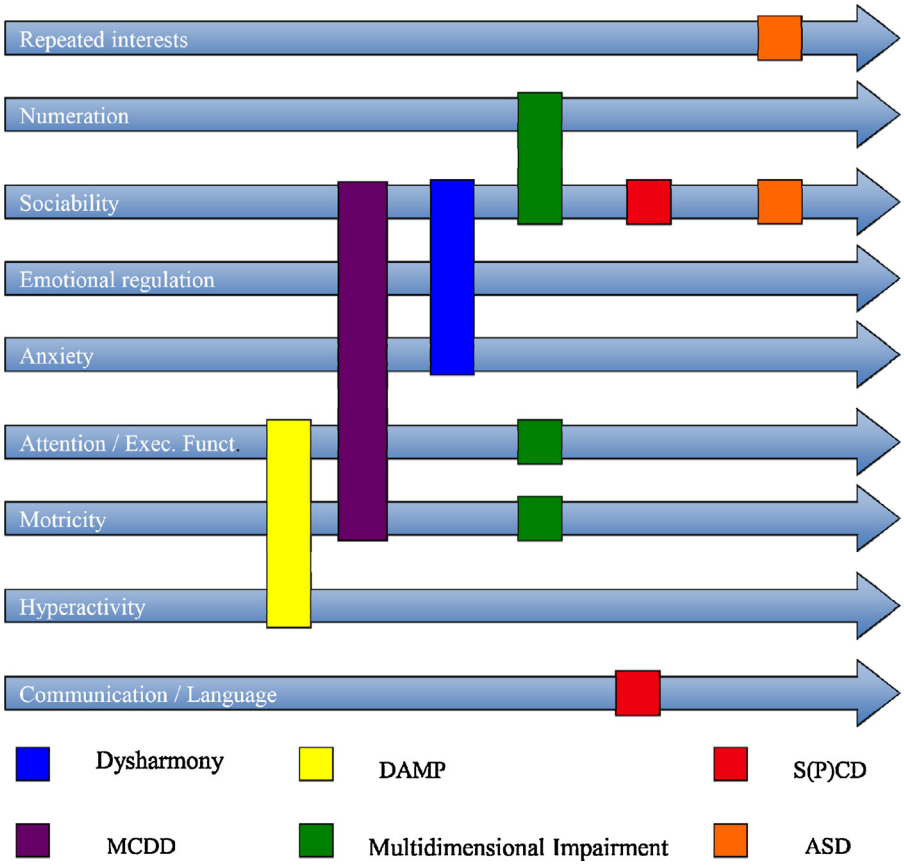

Fig. 1. Phenomenology and developmental lines in DSM-5 Autism Spectrum Disorder and other complex developmental disorders. MCDD: Multi Complex Developmental Disorder; DAMP: Deficit in Attention, Motor control, and Perception; S(P)CD: DSM-5 Social (Pragmatic) Communication Disorder; ASD: DSM-5 Autism Spectrum Disorder.

We argue that a multidimensional approach inscribed in a developmental and integrative perspective, offering a complementary point of view, should encompass the issues posed by the categorical approach. The term integrative refers to the notion that we have to consider child development as formed by the interaction between different dimensions, and that we must put into perspective various complementary influences. Thus, taking into account their innate individual make-up, the child is addressed holistically in their interactions with the environment (family, social, school in particular). The clinician should inquire about their way of life, the different dimensions of their development, the existence of any associated disorders (ex. sensory, visual or auditory), their academic trajectory, and their living environment. In this regard, it is important to understand the place of the disorder and its impact on the individual level as well as on family dynamics.

Future studies must be conducted to examine the validity or the reliability of this dimensional approach. It has the merit of allowing the clinician to have a point of view of the developmental trajectory of each child, knowing that the categorical perspective gives only partial description. Indeed, such a perspective does not, by itself, highlight the different factors (comorbidity features) which, as we mentioned above, are involved in the expression of core symptoms of ASD and which deserve specific medical support. Therapeutically, the dimensional approach, based on a multidisciplinary assessment (Table 2), leads to a functional diagnosis and to a more adjusted medical/cognitive/behavioral/educational treatment. In the case of a child with ASD associated with DCD or/and speech disorder, it is necessary to propose, in addition to the establishment of comprehensive or focused intervention programs (i.e. Early Start Denver Model, Picture Exchange Communication System), a speech therapy and/or an occupational therapy associated with educational facilities.

Several tests or scales commonly applied to children with ASD are given as examples in Table 2. Some focused on specific dimensions whereas others consider comorbidities and dimensional functioning as well as core symptoms of autism. In the first group, the Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 1989) is a semi-structured assessment of the core symptoms of autism. The Dunn's sensory profile (Dunn, 2002) organized into three sections (Sensory processing, Modulation, Behavioral and emotional responses) provide a standard method to measure sensory processing abilities and the effects of sensory processing on functional performance of children. The Aberrant Behavior Checklist (ABC) is a symptom checklist for assessing problem/deviant behaviors of children. In the second group, the Psychoeducational Profile – Third Edition (PEP-3) (Schopler, Reichler, Bashford, Lansing, & Marcus, 1990) was initially built to be used for the development of

Table 2
Multidimensional assessment for a functional diagnosis.

Dimension	Details	Example of instruments
Diagnostic criteria (DSM-5)	Deficits in social communication and social interaction Restrictive repetitive patterns of behavior.	ADOS
General intelligence	Intellectual disability	PEP-3
Specific cognitive dimensions	Attention and executive functions, working memory, processing speed, visual spatial abilities, reasoning, math skills and numeration.	Specific neuropsychological testing
Language	Orofacial praxis, phonology, lexicons, grammar and morphosyntax, semantics, pragmatics and conversational modes, reception/comprehension vs productions/expression.	Specific psycholinguistic testing
Motricity	Motor coordination, fine motor skills, body schema and lateral dominance, temporo-spatial orientation, visual tracking and hand-eye coordination.	Specific occupational therapist testing
Sensory integration	Sensorimotor processing.	Dunn's sensory profile (Dunn, 2002)
Comorbid somatic conditions	Epilepsy, Dysmorphia, Genetic syndrome, Brain size	
Affectivity	Emotion (perception, recognition), temperament, theory of mind, affective empathy, emotional regulation and anxiety	
Deviant behavioral problems	Self-Infurious Behavior, Toileting, Hyperactivity	ABC
Autonomy and social functioning	Communication, Daily Living Skills Socialization, Motor Skills Maladaptive Behavior (Optional)	Vineland

PEP-3: psycho-educational Profile-Revised; ADOS: Autism Diagnostic Observation Schedule; ABC: Aberrant Behavior Checklist; VABS: Vineland Adaptive Behavior Scales.

individualized educational programs within the TEACCH method (Schopler, Mesibov, & Hearsey, 1995). It introduced a developmental approach assessing imitation, perception, fine and gross motor skills, eye-hand integration, cognition, and language. The PEP-3 also identifies degrees of behavioral abnormalities in relating and affect, play and interest in materials, sensory responses, and language. In the same way, the Vineland Adaptive Behavior Scales (VABS) (Sparrow, Cicchetti, & Balla, 2005) evaluates several domains, i.e. communication, daily living skills, socialization, motor skills, and maladaptive behaviors is often used for children with ASD.

5. Conclusion

In the field of autism, successive redefinitions of diagnostic criteria have not succeeded at constraining the complexity of the clinical reality. The flaws of the categorical approach are especially evident for NOS patients and other borderline cases to which many different diagnostic categories both within and outside the DSM classifications can be applied. A multidimensional assessment inscribed in a developmental approach allows clinicians to address the child holistically taking into account their interactive experience with the environment throughout their development, and furthermore, to promote an empathetic relationship with the patient. In this way, clinicians can achieve a functional diagnosis enabling the elaboration of a tailored therapeutic proposal. At the current stage, this proposal is mainly speculative and based on an historical synthesis and some clinicians' experiences (e.g. Lai et al., 2013; Leroy et al., 2010). Future studies must be conducted to examine the validity or the reliability of this dimensional approach. However, this could constitute one of the major challenges in prognosis in terms of everyday life and social inclusion of the ASD patient.

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