



Prototypical autism: New diagnostic criteria and asymmetrical bifurcation model

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ABSTRACT

The current “autism spectrum” DSM 5 diagnostic criteria and autism standardized diagnostic instruments promote considerable heterogeneity or clinical indecision and may be detrimental to the advancement of fundamental research on autism mechanisms. To increase clinical specificity and reorient research towards core autistic presentations, we propose new diagnostic criteria for prototypical autism during the age of 2- to 5-years. We include autism within other non-dominant, familiarly aggregated phenomena sharing asymmetrical developmental bifurcations, such as twin pregnancy, left handedness, and breech presentation/delivery. Following this model, nature, trajectory, and positive/negative signs structure of autism would result from the polarized problem of whether or not language and information is processed in a socially biased manner. Prototypical autism would follow a canonical developmental trajectory by which a gradual decline in social bias in the processing of incoming information, overtly beginning at the end of the first year, bifurcates into a prototypical autistic presentation in the second half of the second year of life. This bifurcation event is followed by a plateau, in which these atypicalities show maximal stringency and distinctiveness, and then ultimately, in most cases, by partial normalization. During the plateau period, the orientation towards, and processing of, information is considerably modified, with an absence of bias for social information, contrasting with a high level of interest in complex, unbiased information, independently of its social or non-social nature. Integrating autism into asymmetrical developmental bifurcations would explain the absence of deleterious neurological and genetic markers and the presence of familial transmission in canonical autistic presentations.

1. Current diagnosis of autism

1.1. Clinical diagnosis

1.1.1. Criteria

Since publication of the DSM 5 in 2013 (American Psychiatric Association, 2013), the categorical diagnosis of autism has been made using identical criteria related to socialization and repetitive behaviors and restrictive interests for all ages of life. An autistic person must show both a reduction in nonverbal aspects of socialization, manifestations of reciprocity, and the ability to initiate relationships, and two of four possible signs in the area of repetitive behaviors and restricted interests: a reaction to change, “sensory” atypia, repetitive use of objects or behaviors, and interests that are unusual in their nature or intensity. Four specifiers describe dimensions that can vary and influence the clinical presentation: intelligence level, language level, comorbidities, and the

level of required support (or severity) in each of the two diagnostic areas. The value of the specifiers does not contribute to the decision of the categorical diagnosis.

The great diversity of clinical presentations allowed by the use of specifiers and polythetic criteria (currently, only for the second area of repetitive behaviors) is indicated by the choice of the term “autism spectrum”. The spectrum and specifiers approach implies that, at a given age, multiple levels of language, need for support (which is distinct from phenotypic stringency), co-morbidity, and verbal and non-verbal intelligence, and multiple types of repetitive behaviors, as well as their combination, are all consistent with the same category.

1.1.2. Benefits

The DSM 5 merged diagnoses that were previously distinct in the DSM IV: classic Kanner-type prototypical presentations with language delay and apparent verbal intellectual disability (autism), individuals of

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average verbal and non-verbal intelligence and broadly typical language level and history (Asperger syndrome), and incomplete presentations of the previous conditions (Pervasive developmental disorder not otherwise specified (PDDNOS)). All were merged into a single spectrum that is still categorically defined. The origin of this decision was based on the fact that the DSM IV subgroups were not reliably identified between different diagnosticians from different continents (Tsai & Ghaziuddin, 2014). In research, the possibility of there being a common familial predisposition to forms of varying severity, language level, and history has favoured their unification (Constantino, 2021). Finally, at the healthcare/assistance level, the *spectrum* diagnosis allows individuals who are only close to the clinical threshold to receive services and promotes a sense of belonging (Pearson et al., 2021), and has been credited with the de-stigmatization of autism, at least its mild forms.

1.1.3. Issues

Overall, the combinatory nature of specifiers and polythetic criteria, projected both in cross-sectional presentation and developmental trajectories, promotes considerable heterogeneity and clinical indecision. The inclusive strategy of the DSM 5 was contemporaneous with the seemingly irreversible and unique growth in the reported prevalence of autism (Zeidan et al., 2022) and did not interrupt the clinical temporal drift initiated in the previous DSM editions (Arvidsson et al., 2018). It favoured the predominance of comorbidity in the differential diagnosis (Rodgaard et al., 2021a). Although the criteria required that signs begin in childhood, it has still allowed diagnoses in adulthood that are increasingly distant from the initial category - which we attribute to the “loss of signal” of autism. The predictive value of the diagnosis on the prognosis is very low (Waizbard-Bartov & Miller, 2023) and the diagnosis does not provide clear indications for subsequent interventions (Mottron & Bzdok, 2022).

1.2. Research diagnoses

1.2.1. Instruments and cohorts

The inconsistency of clinical judgment by clinicians led Catherine Lord's team to create standardized observation and retrospective tools, initially for research, more than 30 years ago. Despite the authors' warnings about the risks of their clinical use, these quickly became “gold standards”, to the point that autism became what the Autism Diagnostic Observation Schedule (ADOS) standardized assessment instrument (Lord et al., 1994) and Autism Diagnostic Interview (ADI) (Lord et al., 1994) describe. Although they have not been updated to follow the changes in the DSM, their implantation in the clinical and research world has become universal, independently of the evolution of the DSM. In parallel, continuous unidimensional scales (Lyll et al., 2022) have been developed that identify autism at the extreme of a continuum of distributed traits. They are used clinically for screening and in research as a component of “continuous” models of autism.

1.2.2. Benefits

The initial benefit was the standardization of research populations. The notion of a spectrum also allows the researcher to gather much larger populations (Frith, 2021). It has also allowed the creation of research cohorts, such as the Simons Simplex Collection (Fischbach & Lord, 2010), which have generated and still generate a very large number of studies.

1.2.3. Issues

The use of standardized instruments did not prevent the increase in the reported prevalence of autism and led to the endorsement of the results acquired on the populations thus diagnosed. Their summary score has been very sensitive to confounding variables, such as the presence of behavioral difficulties (Havdahl et al., 2016). At the research level, the inclusion of autism in the DSM as “autism spectrum disorder”, beyond its assimilation within a disorder that is increasingly questioned

by neurodiversity advocates, presupposes that it can be modeled similarly to other psychiatric conditions, which is debatable. Alternatively, placing autism at the extreme of a unidimensional continuum does not account for the uniqueness of some autistic individuals who share a high degree of similarity in the co-presence of multiple complex individual signs and cognitive profiles (Gagnon et al., 2022). The current situation of an increasing resemblance between individuals diagnosed with autism and the general population (Rodgaard et al., 2019) leads to an increased risk of type two errors. The existence of a very heterogeneous category also pushes scientists to invent chimeric models (for example, including neurodevelopmental populations in autism leads to the search for common final pathways between subjects with very diverse presentations). Finally, the populations thus diagnosed cannot be reliably stratified into sub-groups (Wolfers et al., 2019), which suggests the unity of the spectrum for some (Fombonne, 2020) or the proof of a degree of heterogeneity which defies sub-classification (Mottron & Bzdok, 2020). Such standardization is performed at the risk that the populations thus identified are no longer questioned and considered to be the same, yet heterogeneous, category, thus preventing the isolation of “natural” subcategories within the spectrum.

2. New criteria for prototypical autism

2.1. Rationale

Kanner discovered autism within the diversity of atypical pediatric development to which he was professionally exposed (Kanner, 1943). The clinical, empirical and theoretical stagnation we are facing now justifies the renewal of this seminal gesture, to re-discover “autism” within the autism spectrum. The criteria that we propose here as a new reference point for research and clinical use were formulated from our clinical experience of more than 2000 diagnostic assessments of children before 5 years of age. They aim to describe the children that we judge to be phenotypically highly similar to each other among those who score positive using the DSM 5 and standardized tools.

2.2. Structure of the criteria

The DSM criteria are defined in an abstract and general way, which contributes to the instability and heterogeneity of the population it defines. Our aim is to re-establish a category of prototypical autism as a discernible, rapidly identifiable, unique pattern during the plateau period (period without major language gains, usually in the 2- to 5-years period). After excluding syndromic autism, phenocopies, and sub-threshold individuals, prototypical autism combines: a) a series of signs qualitatively recognizable in isolation, mostly related to the detection and processing of complex perceptual information (e.g., longer visual inspection/rotation of tridimensional objects), b) a contrast between intact abilities (e.g., walking age; Kuo et al., 2022) and functions not developing at a typical age (one to two-year plateau in the 2- to 5-years period without oral language; Gagnon et al., 2021), c) the absence of markers for neurodevelopmental impairment (non-verbal intellectual disability, Courchesne et al., 2015; epilepsy, Amiet et al., 2008; or identifiable pathogenic mutations, Tammimies et al., 2015), d) a behavioral ratio between the overt interest in perceptual and social material skewed towards non-social material (Mottron et al., 2006), e) an absence of bias for social information (Nystrom et al., 2019), contrasting with expertise/superiority for perceptual processing (Kaldy et al., 2011), f) a pronounced sex ratio in favor of males (Zeidan et al., 2022), and g) macrocephaly (Sacco et al., 2015).

2.3. Specifying specifiers

The notion of a specifier has multiple implications with respect to the promotion of heterogeneity within the “spectrum” thus defined. First, the values taken by specifiers can modify the presentation of each sign

by which the condition is identified, blurring the delineation of their qualitative prototypical form. Second, each specifier represents a degree of freedom of a continuous variable, leading to the “dimensional” dissolution of the partition between autism and non-autism. Unidimensional instruments, such as the AQ (Baron-Cohen et al., 2001) or SRS (Constantino et al., 2003), reduce autism to the dimension they measure, thus creating the dimensional property of what they measure. This position leads to an interpretation of autism as being intertwined with almost all psychiatric conditions; however, “autistic traits” measured by these instruments are not autistic but rather social traits (Mottron & Bzdok, 2020). The current “spectrum”, which posits heterogeneity as a dogma, inevitably leads to the secondary dissolution of its initial recognition. It prevents and discourages its rediscovery. The autism spectrum is gradually identifying with the entire family of neurodevelopmental disorders. This situation demands a new recognition-definition-investigation cycle within the current DSM 5 spectrum (Mottron, 2021b), beginning with new criteria intended to replace “profound autism” (Waizbard-Bartov et al., 2023) with “prototypical autism”.

2.4. Proposed new criteria for prototypical autism

CLINICAL JUDGMENT
Rapid and certain recognition as autistic (for expert clinicians) Could be used to teach how to recognize autism to non-experts
LACK OF NEUROGENETIC ASSOCIATIONS
Non-delayed early neurodevelopmental milestones (e.g., walking), excluding language and toilet training Sectors of motor integrity (excluding atypical gait) Indirect indications of normal non-verbal intelligence Apparent neurological and genetic integrity (e.g., no external or internal dysmorphism, epilepsy, or identified CNV or neurogenetic condition)
DEVELOPPEMENTAL COURSE
Atypia detected by an adult before 2 years of age Regression of vocabulary during the second year or a delay in its emergence Abrupt change of overt typical socially oriented behaviors during the second half of the second year of life
MAJOR, PROLONGED, RECOGNIZABLE LIMITATIONS OF SOCIALLY DIRECTED BEHAVIORS
A1. Reduced overt socio-emotional reciprocity in Synchronous reactions to oral and gestural addresses by the adult Initiation of shared socially oriented activities with peers Initiation and maintenance of interactions with adults (gaze, pointing, and vocalizations) Responses to the adults' initiation of shared or collaborative activities (e.g., pushes back the forearm of the person interfering with their activity) Overt sharing of pleasure in a non-physical activity, with intact pleasure in physical activities
A2. Marked reduced/atypical non-verbal relational features in Facial expression (e.g., a mostly serious face) Synchronic voice/face expression/vocal utterances Hand leading, face-orienting, body-pushing to make demands “Control gaze” and body orientation towards peers
A3. Marked reduced long-term relationships with peers, as indicated by Unsuccessful recurrent overtures with peers Absence of overt preference for a familial over a non-familial peer Indifference or absence of child-mothering behaviors with younger children
MAJOR, PROLONGED, AND RECOGNIZABLE ATYPICALITIES IN NON-SOCIALLY DIRECTED BEHAVIORS
B1. Repetitive movements and use of objects, such as

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MAJOR, PROLONGED, AND RECOGNIZABLE ATYPICALITIES IN NON-SOCIALLY DIRECTED BEHAVIORS
Alignment, classification, embedding, transfer, or throwing of objects that is repetitive and recurrent in their form Repetitive and recurring finger movements Keeping an object in the hands for long periods of time
B2. Recurrent and recognizable atypical emotional reaction to change, such as Tantrum when certain aspects of the environment or action taken by the child changes, ending abruptly when resolved Flapping, jumping on the spot, or recurrent tensing of the limbs during positive emotions, constant in its form Food selectivity, leading to significant family discomfort
B3. Intense and prolonged interest in A particular class of objects (e.g., letters and numbers), domain, (e.g., animals), or dimension (e.g., rotatory objects) Actions with inanimate objects predominate over those involving animate representatives
B4. Recurrent/prolonged perception-based behaviors, such as Hands over ears to noises or voice, elbows forward Three-dimensional inspection of objects or hands Repetitive noise produced with objects Lateral and/or obstructed gaze
LANGUAGE
Non-verbal or minimally verbal plateau of communicative language, of at least several months delay before language emergence or plateau after a language regression Repetitive or varied but recurrent, atypical, non-communicative vocalizations Follows simple instructions during the non-verbal plateau Self-taught learning of a vocabulary after the plateau period in a language other than that spoken by parents and peers Recurrent and non-communicative naming of numbers/letters or objects significantly ahead of communicative speech acts Recurrent use of statements of which the caregivers recognize the origin (delayed echolalia) Recurring immediate echolalia of parts of dialogue not addressed to him Prolonged personal pronoun or possessive adjective reversal

2.5. Analytical framework for the prototypical criteria

In its current state of development, this list of signs does not include a quantitative threshold of a summary score. The final diagnostic decision remains that of the clinician. It should be used in association with an overall prototypicality ranking of individuals according to their similarity with a subjective prototypicality judgment. This judgment can be quantified by ranking how certain the clinician is of the diagnosis, how rapidly the child was recognized as being autistic, how similar the child is (both cross-sectionally and longitudinally) to the expert's own representation of autism, and how much this could be used to teach autism to non-experts. Such recognition, or diagnostic certainty, is equal or superior to that resulting from polythetic criteria (Barbaresi et al., 2022; de Marchena & Miller, 2017). It distinguishes between severity (significance of adaptive difficulties) and prototypicality (identification of the particularities of the child as autistic), making the prototypicality prevail in the diagnosis.

2.6. Clinical advantages

We predict that the combination of a qualitative description of signs, clinician exposure to an enriched population, and multiplication of information sources have more clinical benefits than the current use of a polythetic threshold, standardized instruments, and abstractly defined signs. This analytical framework allows ranking in prototypicality children with a DSM 5 ASD diagnosis in the period of 2- to 5-years of age from the material available to clinicians during their evaluation, regardless of the source (interviewing caregivers, file survey, observations in daycare, ADOS). It considerably restricts the prevalence of individuals satisfying the DSM 5 criteria, while temporarily benefiting

from their universal aspect. It makes it possible to distinguish between an orientation towards services highly determined by the autistic condition from services that are determined, above all, by the needs and not the diagnosis. The application of these criteria and analytical framework to ambiguous clinical situations should make it possible to orient the diagnostic decision towards alternative solutions to the diagnosis of autism, even in cases in which the child quantitatively satisfies the current DSM criteria.

3. Model grounding new autism criteria: autism as an asymmetrical bifurcation

3.1. Changing the paradigm

Here, we develop the hypothesis that to account for the phenotypic and biological traits that constitute autism, it is necessary to change the type of biological object – here, psychiatric/neurodevelopmental conditions - with which it is grouped. The assumption that autism is the same type of biological entity as most other psychiatric or neurodevelopmental conditions should be abandoned. Subsequently, we should enlarge the disciplines from which we borrow the conceptual frameworks and empirical instructions to model autism. We propose the reconceptualization of autism as the non-dominant branch of a developmental bifurcation, as are other non-dominant branches in two-state (of highly polarized) outcomes, such as left-handedness for lateralization, twin pregnancy for fecundation, and breech presentation and delivery (BP/BD) in late pregnancy.

We first show how the contrast of “negative” social signs and “positive” non-social signs provides a meaningful, economical, and rational structure for the signs that characterize autism at its beginning, as well as to its biological markers (or absence thereof). We then show how the absence of biomarkers makes it necessary to abandon deleterious mutations as a guide for modeling the neurobiological mechanisms that result in an autistic trajectory. We then present how the longitudinal trajectory in prototypical forms follows a bifurcation scheme with a bayonet-shaped morphology. Finally, we expose how the processing of environmental information with or without a social bias may act as the splitting factor in the polarized system that governs the interaction between developing individuals and their informational environment, determining the characteristics of the canonical autistic presentation and trajectory.

3.2. Negative social signs and positive non-social signs

The reduction in orientation and social response behaviors is at the very origin of the term autism and has formed the heart of the condition since its inception (Kanner, 1943). It constitutes the non-polythetic section A (A1 to A3) of the DSM 5 criteria. The A1, A2, and A3 signs are essential for the recognition of autism in the period before 5 years of age, even if multiple conditions can (pheno) copy them. These are, on the whole, mostly negative signs, thus, behaviors that typically-developing children exhibit and autistics do not. Although there is still significant progress to be made in determining possible endophenotypes common to the three types of “deficits” inventoried by the DSM IV in the social interaction area (Forgeot d’Arc & Mottron, 2012), we have included them in our criteria, while specifying them qualitatively when possible, because they are neither contested nor debatable.

On the other hand, the position of “repetitive behaviors and restricted interests” in the diagnosis, as in the modeling, of autism is much less consensual. Their identification as “repetitive” is not very specific and poorly distinguishes between repetition by the impoverishment (Bodfish et al., 2000) of input or processing from what would be specific to autism itself. These are mostly “positive” signs, thus behaviors that autistic children exhibit that typically-developing children do not, or at least not at this level of frequency, duration, or in multiple qualitative aspects.

We have discussed elsewhere how (Mottron et al., 2006) a large part of repetitive behaviors can originate from perceptual over-functioning, well beyond the sensory aspects of the DSM 5 B4 sign, which under-specifies their forms and functions (Mottron, 2019). An atypical imbalance of interest towards the physical, perceptual, or informational properties of the surrounding world without social bias dominates autistic interests before 5 years of age, as highlighted by the enhanced performance, role, and autonomy of perception (Mottron et al., 2006, 2009, 2013). All experts with exposure to prototypical autistic children at the period of 2- to 5-years of age are aware of how these children are immediately interested in what is present in the room, including what they are being shown by the examiner, but without overtly displaying joint attention, shared enjoyment, or, more generally, to-and-fro interactions related to these objects with the surrounding peers and adults. Repetitive behaviors do not diminish exploration and curiosity about the world, as we demonstrated empirically (Jacques et al., 2018). On the contrary, they demonstrate an orientation towards complex perceptual incoming information, without a social bias. The “repetitive behaviors and restricted interests” signs could be re-conceptualized as “enhanced, perception-based behaviors”.

3.3. Bayonet-shaped development as an organizer of the autistic trajectory

3.3.1. Overall developmental trajectory

Autism first signs are becoming visible between 18 and 20 months of age in most cases (Landa et al., 2013). They are preceded by sub-clinical signs that are usually undetectable, except in targeted, sib-pair prospective studies (Ozonoff et al., 2010). There is, thus, a narrow time-window, unique from other conditions, in which the precursor signs transform into the onset of the majority of noticeable and recognizable signs. This developmental sequence is particularly clear for bayonet-shaped language development (Gagnon et al., 2021), which includes early language onset, regression, a plateau, and a certain level of language recovery. See Fig. 1 for a schematic representation of the bayonet-shaped language development. The plateau is followed by extremely variable and unpredictable outcomes, ranging from an “optimal outcome” to non-verbality in adulthood, with an overall relative normalization – albeit extremely variable - of positive and negative signs after 5- to 6-years of age (Fecteau et al., 2003; Piven et al., 1996; Simonoff et al., 2020).

3.3.2. The invisible period

Prior to one year of age, autism remains undetectable by parents and clinicians in a large majority of cases. Around the end of the first year of

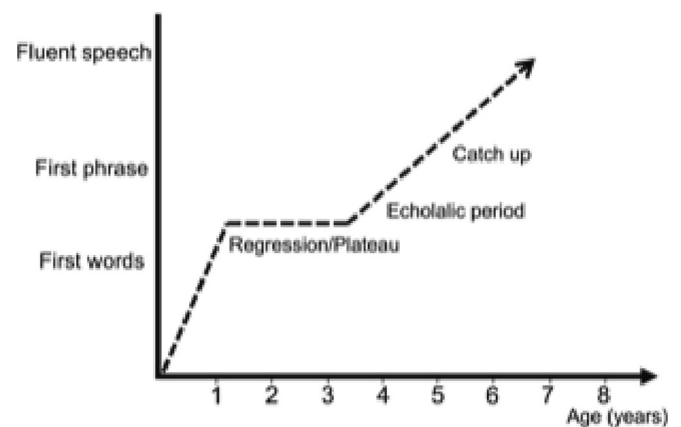


Fig. 1. Schematic representation of the bayonet-shaped language development: an early language onset is followed by a regression and a developmental plateau, then by a certain level of language recovery. Mostly derived from the data reported by Gagnon et al. (2021).

life (Ozonoff et al., 2010; Zwaigenbaum et al., 2005), subtle atypicalities in information processing gradually and then abruptly distinguish a subset of individuals “at risk” of subsequently presenting an autistic phenotype. These slight variations can be measured or noticed in prospective studies (Ozonoff et al., 2018; Webb & Jones, 2009) but poorly predict subsequent development. Neurobiological differences may be present during this period and associated with the later diagnosis of autism, but their impact on cognition and behavior may be non-specific (Varcin & Jeste, 2017).

By mapping these predisposing phenomena on the two diagnostic domains of DSM 5 that characterize autistic individuals, it is possible to contrast their social and non-social components and course. Discrete manifestations of the enhanced importance of the perceptual dimension of the environment, independently of its social value (reward, context, and consequences) become increasingly visible (Freschl et al., 2021; Ozonoff, Macari, et al., 2008). The children display a prolonged fixation on environmental targets, without privileging social content (Wang et al., 2018), the repetitive manipulation and orientation of objects (Miller et al., 2021), particularly complex ones (Manyakov et al., 2018; Moore et al., 2018; Pierce et al., 2016), and longer periods of visual exploration of objects (Elsabbagh et al., 2013) and parts of the face (Moriuchi et al., 2017). This last aspect is a paradigmatic example of a perception-based interest in the world, regardless of whether or not it is presented by a person. This contrasts with the gradual, then abrupt decrease in social processing bias, as manifested by decreased interest (orientation, reaction, initiative) in the social dimensions of the same environment (Ozonoff & Iosif, 2019). From the age of 12 months, autistic children gradually display fewer and fewer of the behaviors considered to be essential for socially oriented communication in typically-developing children. Their attention to human faces and reactions to voices decreases (Bhat et al., 2010) and they display a significant reduction in joint attention and a decline in gazing towards faces over time (Gangi et al., 2021).

3.3.3. Bifurcation/plateau

Data from prospective studies have shown overt regression at approximately 18 months of age or a developmental plateau at the same age, which are major constituents of the autistic phenotype, occurring in up to 88 % of individuals with strictly defined autism (Boterberg et al., 2019; Ozonoff & Iosif, 2019). Overt, parent-detected manifestations of prototypical autism occur within a specific time window, the second half of the second year of life (Ozonoff et al., 2018; Ozonoff, Heung, et al., 2008; Zwaigenbaum et al., 2007). The abrupt emergence (Green, 2022) of: a) behaviors demonstrating a decrease in social bias, b) behaviors showing an enhancement of the performance, role, and autonomy of perception, and c) language regression *broadly coincide in time*. The inflection of the socio-communicative developmental curve is crucial, it represents a developmental bifurcation corresponding to the overt regression reported in retrospective studies. Socially oriented initiatives and responses and manifestations of synchrony with peers and adults are drastically reduced and limited to basic needs. From this point on, the perception and manipulation of complex visual-spatial and auditory structures predominate, such as atypical inspection of movements and alignments, and orientation towards perceptually defined categories of objects or patterns, such as letters and numbers. “Regression” can be reconceptualised as the abrupt transition from predisposition to condition.

During this plateau period, which lasts from approximately 6 months to several years (Gagnon et al., 2021), autistic signs are at their maximum (Courchesne et al., 2021). The social/non-social hierarchy of information orientation and processing is considerably modified, with an absence of bias for social information, contrasting with a greater interest in complex information, independently of its social or non-social nature. The three components (social, non-social, and language) of the bifurcation at 18 months correspond to a domain-general re-ordering of cognition in favor of complex, non-socially biased, perceptual material.

This reorientation, independent of social gratification, culminates in intense interests and peaks of ability or precocity in the processing of certain types of information according to the enhanced perceptual functioning model (Mottron et al., 2006). During the plateau period, negative social and language signs are stable, with minimal progress in language/communication or orientation towards animate subjects, but an increase in vocabulary labelling of familial categories could be observed (Ostrolenk et al., 2017). During this period, the repetitive signs increase in importance, with a focus on non-socially presented language (Kaldy et al., 2011; Kissine et al., 2018; Ostrolenk et al., 2017).

3.3.4. Outcome

After a period of disinterest in socially oriented oral language, there is a delayed revival of language through the non-linguistic processing of language (Mottron et al., 2021). Partial normalization of autistic social characteristics occur in adulthood, although the reduction in social bias remains empirically detectable: cognitively, autistic adults still process gaze-based cues for the same duration as arrow-based cues, whereas gaze-based cues are processed for longer by typical people (see (Vlamings et al., 2005) for a review and relevant findings); autistic gaze orientation is still mediated by how frequently the presence of the target to be detected is predicted, whereas typical people follow the direction of the gaze regardless of its predictive value – a paradigmatic example of social bias; an emphasis on structural regularities rather than social content enables autistic individuals to outperform typically developing participants under non-predictive conditions (Ristic et al., 2005); older autistic individuals continue to display decreases in desirability bias, emotional contagiousness, and the priority given to social expectations and reputation, but their basic mechanisms of mimetic desire (Forgeot d'Arc et al., 2016; Vinckier et al., 2021) and social motivation (Chevallier et al., 2013; Jaswal & Akhtar, 2018) are unremarkable.

We highlight here the contrast between the prototypical nature of the plateau presentation and the variability of its outcome. The outcome of the plateau period is unpredictable; the same phenotype may develop into an almost complete recovery of language and adaptive skills (Fein et al., 2013; Pickles et al., 2014), with few qualitative differences relative to typical individuals, or may remain heavily altered in a small fraction of individuals (Tager-Flusberg & Kasari, 2013).

3.4. Absence of biomarkers as a diagnostic criteria

The search for a cause of autism according to a medical model — a cascade effect of a circumscribed event or defect — has prevented a series of null results from being given their full theoretical importance (for a detail empirical support of this statement, see Rabot et al., 2023). Indeed, it is the association between the *absence of atypia in certain domains* with a recognizable behavioral phenotype that underlies the clinical definition and distinctiveness of autism in its prototypical form. It is time to accept the heuristic and modeling consequences: the most stringent and homogeneous autistic phenotype is not associated with neurobiological/neurogenetic defects. Maintaining that we are on the verge of discovering these neurobiological/neurogenetic defects in spite of the negative evidence is sterile. The absence of a neurobiological/neurogenetic defects leads to the conceptualization of autism as a “biological developmental possibility”.

We suggest that in conditions in which an identified neurogenetic condition is reported to increase the risk of autism, the level of similarity to prototypical autism is either low or trivial. Thus, in cases of large deletions, a) the contribution to obtaining a phenotype judged to be autistic is based, above all, on a lowered IQ and not on strictly “autistic” signs (Douard et al., 2020); b) When we can measure how similar a clinical trait in prototypical autism is with its hypothesized equivalent in a specified condition, the distribution is bimodal: this is, for example, true for macrocephaly associated with mutations in the gene encoding phosphatase and tensin homolog (PTEN). There is indeed a clear difference between extreme macrocephaly, often greater than three SD for

PTEN, versus macrocephaly around the 97th percentile in autism, and this contrast predicts neurobehavioral differences (Busch et al., 2019); c) For Fragile X, in which phenotypic differences with the prototype have been well studied, there are measurable differences on standardized scales between autistic subjects with and without Fragile X (Hall et al., 2010; Klusek et al., 2018; McDuffie et al., 2015; Wolff et al., 2012); d) for Neurofibromatosis 1 (NF1), “autism” scores are not affected by phenotypic alterations identical to those found in autism, but by Attention deficit hyperactivity disorder (ADHD) features (Fombonne et al., 2020). Finally, if we do not rule out the possibility of a sporadic association between prototypical autism and identifiable neurogenetic conditions, the heuristic value of this association may not exceed that of an association by chance, insufficient to draw conclusions about autism from animal models based on a tenuous similarity with non-syndromic autism of deleterious mutation phenotypes (Silverman et al., 2022).

The absence of deleterious mutations among individuals with the most homogeneous, and recognizable autistic phenotype (Wickstrom et al., 2021) with strong evidence of familial transmission is one of the characteristics of autism from which we can recast the phenotype within the current spectrum. It is consistent with the dominant absence of gross structural brain abnormalities and the two main comorbidities of developmental brain damage in prototypical autism: non-verbal intellectual delay and epilepsy (Liu et al., 2022). By contrast, these markers are strongly associated with “syndromic” forms of autism accompanying identified neurodevelopmental conditions that are phenotypically distinct from autism (Amiet et al., 2008; Moss & Howlin, 2009).

Clinically, neurodevelopmental integrity is manifested by two major null findings which are dominant features of prototypical autism: the rarity of a significant delay in walking (Havdahl et al., 2021) and a normal or minimally reduced non-verbal IQ (Courchesne et al., 2015). Importantly, this focus on a series of null findings should not be understood as a drift towards a less stringent phenotype of “autistic traits”. Prototypicality may be orthogonal to severity, but parallel to distinctiveness.

3.5. Asymmetrical bifurcations in neurodevelopmental pathways

Certain non-dominant neurodevelopmental pathway or organization bifurcations are not diseases. They represent stable, although unequally distributed, solutions of a highly polarized or dichotomous dynamic biological system. This is the case for left-handedness, twin pregnancy, breech presentations (BP), brain lateralization and gender identification. Here, we present the breech presentation-delivery (BD)/autism analogy. In the context in which anatomical constraints and developmental pressure allow mostly two outcomes (cephalic delivery or BD) and after a period during which the presentation outcome is flexible, irreversible BP occurs in 3 to 5 % of pregnancies. Multiple factors, differing according to gestational age, favor this outcome. Most are familial, influenced by continuous traits or features under polygenic influence (size and shape of the uterus, size of the mother and child, prematurity, twin pregnancy, and the familial occurrence of BP) (Nordtveit et al., 2008). Others are favoured by “adjunct” factors acting de novo (previous caesarean section, preterm premature membrane rupture, oligohydramnios, low birth weight, and congenital abnormalities) (Toijonen et al., 2020), which, as in autism, can be identified as “syndromic” forms. Such familial and adjunct factors act additively to orient the event, which is no longer “dimensional” once triggered; there is essentially no third choice between cephalic presentation and BP.

We propose that, in autism, as in other non-dominant pathways taken in asymmetrical developmental bifurcations, a stochastic combination of events and genetic constraints, acting additively, may result in the orientation towards the rarer of two possible pathways. These non-dominant orientations are compatible with unaltered organization, neurophysiology, and neuroanatomy, and are therefore virtually contained in the organism in which they occur. They represent recurrent divergences in human development and should therefore be clearly

distinguished from diseases or “biological errors”.

Another common property of such bifurcations is that, while they are events that may influence the entire life of the organism that occur in a fundamentally normal individual, some instances may be associated with a certain number of negative outcomes, adaptive issues/benefits, or disrespect from dominant individuals. In our leading example, BP was frequently lethal in the past, but in its best outcome was consistent with further survival without “biomarkers” or mis-adaptation. In each of these bifurcations, taking the alternative path is followed by a slow and unpredictable return to the adaptive abilities of the more frequent pathway, with consequences of various degrees of having taken the lateral path. These range from mostly complete typical pathways (Breech delivery, after birth), to stabilised atypicalities (left handedness). The return to dominance is such that an a posteriori investigation of individuals who have passed such a bifurcation may not allow the reconstruction of its mechanism, or even reveal its traces. This is the case of the so-called “optimal outcome” in autism. At the same time, the phenomenological homogeneity of the non-dominant path at its prototypical phase contrasts with its quasi-random, or at least unpredictable, outcome.

The bifurcation choice is a homogeneous, highly polarized (and for some, dichotomous) forked pathway within a developmental organism at a certain time in its development. Present neuroanatomical or neurophysiological elements determine their quasi-categorical status as a biological entity/event. Although in some (e.g.: handedness), intermediate, fuzzy, or “fluid” situations are far from exceptional, all remain polarized: dichotomous choices are more stable than intermediate ones. Variations within each dichotomy (e.g., subtypes of breech delivery) or between a dichotomy and other situations (e.g., triplet pregnancies) are either subordinate to the main dichotomy or extremely rare.

These bifurcations are not disturbances that generate noise in a dominant pattern; they have a biological existence of their own. They do not consist of an order vs. disorder opposition, but rather of an opposition between two ordered states. The two alternative paths contrast almost “binary” recognizable phenotypes, despite the infinite variety of independent factors acting additively to favor orientation towards one branch of the bifurcation or the other.

The genetic determinants of developmental bifurcations shed little light on the nature, mechanical constraints, or, more generally, phenomenology of the non-dominant pathway of the bifurcation. Common variants that push development towards one branch or the other are, by definition, common and non-specific, as well as familial. However, despite our ignorance of the number and nature of factors that favor such bifurcations, we can affirm that such conditions are genetically determined, combining the effect of common variants (Armour et al., 2014; Zietsch et al., 2021), as they occur in families, but more frequently in association with “syndromic” conditions (Brandler & Paracchini, 2014; Nordtveit et al., 2008) for all of them.

3.6. Modeling the longitudinal autistic phenotype as a bifurcation of socially and non-socially biased interactions with the informational environment

3.6.1. Biased and unbiased processing

Two complementary forces govern the items of information towards which children direct their attention and interest (Thom, 1983). The first force, typically dominant, in this polarized system can be called “socially biased processing” and the other, “non-socially biased processing”. Social bias is a genetically determined automatic *preferential* interest, from the beginning of development, in what our caregivers and peers are interested in or value. Social bias is the added cognitive and emotional value of shared/synchronized interests and behaviors with peers, as opposed to the “raw” value of unbiased environmental information. This bias implies that both social and non-social information can be processed, but with different degrees of prioritization.

Importantly, social bias differs from social motivation (Jaswal &

Akhtar, 2018). Social motivation encompasses basic species-specific orientation and includes facial perception, emotional processing, attachment, and sexual drive. These mechanisms all function typically in autism, even if they may ultimately be affected by differences in life trajectory and information exposure. The absence of social bias cannot be strictly attributed to a deficit in facial perception (Guillon et al., 2016; Jemel et al., 2006; Palomo et al., 2022), abnormal attachment (Cossette-Cote et al., 2021), or defective attentional mechanisms (Fischer et al., 2016). In typically-developing children, social bias can be quantified and rendered objective by measuring the high proportion of joint attention and pointing in interactions with adults (Tomasello et al., 2007) and of the spontaneous imitation of peers (Nadel, 2015). Clinically, it can be operationalized by zero scores on a social-communicative subscale of the ADOS modules 1 and 2 (standardized diagnostic assessment modules for minimally verbal children).

Conversely, autistic children display a dominant orientation towards information, mostly independently of what their family and peers present to them or use for interactions with them. Empirically, in an experiment in which individuals have to orient their gaze either towards the direction indicated by eye orientation or an arrow, social bias in typical adults is manifested by more rapid looking in the direction that the eyes are looking than in the direction of arrow-target congruent objects (Ristic et al., 2005). How this non-socially biased orientation towards complex structures can economically explain the non-social learning of language and savant abilities has been presented elsewhere (Mottron et al., 2021).

These two forces essentially compete to direct the attention of the child and enrich a brain-behavior cycle. The displacement within the information encountered may be oriented or biased by a social attractor, in which case the child's attention is directed towards what relates to the other person, or it may not, in which case information processing is prioritized according to its intrinsic, unbiased properties. Typical processing shows a hierarchical relationship between the two forces: children may be oriented towards and may process all the information encountered, but positive emotion and motivation is maximal for what is shared with the other person or that maintains a close relationship with the other person, such as speaking the same language (for a review see Chevallier et al., 2012).

3.6.2. The autistic bifurcation

According to our model, the time at which autistic signs become visible coincides with the moment at which this priority relationship is inverted. Whether it is because the social element does not function as an experience or does not exist as a motivation, or because the perceptual salience of the information encountered is greater, the result is the same: the treatment of information, as such, without social bias, becomes dominant. The group intervention studies of Green and colleagues (e.g., Whitehouse et al., 2021), which maximized synchronous experiences in pre- and post-diagnosis children, suggest a lack of social reward or experienced embeddedness as a prime mover that drives this bifurcation. We can indeed act on social bias and elicit an (limited) effect on all autistic manifestations. Our work suggests a growing interest in perceptual information, as such, to be an alternative splitting factor. An unequal ratio between perceptual processing and the rest of cognition in favor of perceptual processing (Caron et al., 2006), the possibility of a difference in plasticity between men and women (Mottron et al., 2015), and the non-social learning of language (Ostrolenk et al., 2017) are consistent with the second interpretation. Nonetheless, both interpretations are consistent with the model and can coexist. They could even be interdependent. In both cases, the pre-plateau period can be interpreted as one in which one force gradually decreases and the other gradually increases, until a threshold corresponding to the bifurcation point is reached.

We suggest that the bifurcation of a *normal* genetic program (thus, without major alterations, as stated above), which typically involves the hierarchical intersection of environmental information processing and

social bias, readily models the combination of the absence of neurobiological findings with the autistic behavioral and cognitive phenotype and language delay. Accordingly, our innate linguistic ability is typically triggered by synchronized, shared, and interactive collaborative activities (Tomasello, 2020). This appears not to be the case for autistic individuals, who display mostly non-social delayed oral language acquisition (Mottron et al., 2021). Autism may therefore represent an alternative socially *unbiased* orientation towards, and processing of, *similar* environmental, social, non-social, and linguistic information with an *intact* neurocognitive apparatus, but one which is unbiased towards social information.

3.7. Explanatory value of the model

Our model has an explanatory value for several central issues in autism. First, it can explain why the most marked forms of autism combine a relatively constant lifelong trajectory, despite considerable variation in its outcome, with rare, but demonstrated almost complete subsequent normalization. Second, it allows the contrast between mostly reduced socially oriented behaviors and mostly enhanced information- and object-oriented behaviors. Third, it accounts for strong heritability, but supported only by multiple common variants shared with other conditions. Fourth, the model allows that a strongly atypical presentation can contrast with small or inconsistent effect sizes of biomarkers. Fifth, it recognizes widespread domain-specific alterations to information processing, despite the absence of uncontested heritable endophenotypes. Sixth, it is informed by the presence of sometimes exceptional abilities. Seventh, it models incomplete forms of the condition as predisposing factors, as developmental transformations, or, in the case of Asperger's, as a result of the bifurcation occurring after language acquisition. Eighth, the model considers the predisposing role of a neurodevelopmental condition for non-prototypical syndromic forms.

4. Neurodivergent issues

There have been concerns that advocating for an autism prototype cancels the societal advances pertaining to neurodiversity (Pearson et al., 2021). We claim the opposite. Currently, science is still mostly searching for defects to explain autism, such as genetic "errors" as a model (e.g., Chan et al., 2022), or reducing the alterity of autism to the extreme of a quantitative trait (Constantino et al., 2021). We strongly claim that the practical results of such intellectual posturing is to negate the radical alterity of the needs and learning modes of prototypical autism, which may radically differ from those of non-autistics. Alternatively, integrating autism within the category of variants identified as asymmetrical bifurcations radically distinguishes it from being a biological error, regardless of the detrimental consequences it may have on the person's quality of life. Disentangling severity and prototypicality (sometimes overlapping, sometimes orthogonal), emphasizes that autistic individuals may require anything from no to major support, while being both profoundly different and profoundly similar to typical humans.

5. Future directions

Several future studies stem from this criteria and analytical framework; First, in order to turn this list of signs into a consensual diagnostic grid, we have initiated with an international group of experts exposed, as a group, to more than 10,000 children referred for a possible autism diagnosis a "weighting" study, which should provide information on the respective contribution of each of its components to diagnostic certainty. This project allow the construction of an instrument that integrates the resulting differential weights of qualitatively defined autistic signs, in which highly weighted signs are scored more than lowly weighted ones. It aims to replace validation with a consensus between

the categorical judgment of experts and a threshold score by the recognition of prototypical signs and their combination in early years.

Second, this instrument could be used to rank individuals in populations enriched in autism from the most to the least prototypical. Such an instrument allow the identification of a large number of children who exhibit these signs in their entirety, or nearly so, from different experts and recruitment sites. The application of this instrument to a large number of children with a diagnosis of ASD according to DSM 5 definition make it possible to measure the distribution of each of the signs taken separately, as well as the distribution of their number that are simultaneously found in each individual. We predict that this will reveal a discontinuous distribution of the number of traits. A bimodal distribution of the signs will support the hypothesis that the current heterogeneity of the autistic spectrum results from grouping individuals unequally similar to each other, including a subgroup of highly similar individuals (with a greater copresence of qualitatively identified signs) from which the science of autism can re-emerge (Mottron, 2021a, 2021b; Mottron & Bzdok, 2020). Such a result would empirically demonstrate that the “continuous distribution of traits” as concluded from “trait studies” (Constantino et al., 2003; Kamio et al., 2013) is instrument-based and does not capture the true nature of autism.

Third, the use of arbitrarily truncated populations in case-control cohorts of highly similar prototypical individuals identified by an instrument that selects qualitative signs according to their weight should be more informative concerning autism than relying on cohorts of hundreds of thousands of individuals identified by “trait”-standardized instruments, particularly when the diagnoses are obtained as adults (e. g., Warrier et al., 2020; see Rodgaard et al., 2021b, 2022 for supportive data). Turning the research community towards a strictly defined category, both positively and negatively, including the characteristics of trajectories, should bring together cohorts of individuals in numbers and at a level of similarity that exclude their simply being a result of a “convenience sample” or chance. Such a number and level of similarity demonstrate de facto that prototypical autism is a natural category (see Frazier et al., 2023 for decisive support of this prediction). Once validated by their very existence, such cohorts and the biological results that would be obtained with them (genetics and imaging) can serve as an anchor point to determine the true heterogeneity of autism (for example, that of the outcome in adulthood from an identical picture during childhood), as well as true comorbidity (and not that based on diagnostic confusion, Rabot et al., 2023).

6. Conclusion

In this paper, we present a strong hypothesis about the nature of biological variation that is autism, which definitely links it to humanity in a less ambiguous manner than the notion of neurodiversity. We propose that autism in its prototypical form is neither a spectrum nor a disorder, but rather a human possibility. Integrating autism in such asymmetrical bifurcations can account for multiple characteristics of autistic development in its prototypical form. We also provide new criteria of prototypical autism as a premise to be able to falsify the model we propose. Right- and left-handedness, twin pregnancies, and non-cephalic delivery are stable variations of human life, and so is autism.

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Declaration of competing interest

None.

Data availability

No data was used for the research described in the article.

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