

Conceptualizing Autism: The Role for Emergence

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THE COMPONENT, FRACTIONABLE APPROACH TO AUTISM

Most behavioral, neurobiological, and genetic research has approached autism categorically. However, over the years, a number of researchers have suggested that autism may be better understood by examining the component behavioral and cognitive abnormalities (reviewed in detail elsewhere¹). In 1971, Wing and Wing² stated that the “multiple impairments (of autism) can vary in severity and...can occur independently in various childhood conditions.” In 1989, Goodman³ posed the question: “Infantile autism: a syndrome of multiple primary deficits?” In 1996, McBride and colleagues⁴ argued for a more dimensional approach, saying “...the components can be considered individually,” and that there should be a “consideration of the interactions between domains.” The multi-dimensional perspective is reflected in the increasing use of the terms such as “autism spectrum” and “broader autism phenotype.”

Recently, Happe and colleagues⁵ reviewed the compelling case for considering the autism spectrum disorders from a component perspective and used the term *fractionable* to emphasize this point. They pointed to accumulating evidence suggesting that alterations in the defining triad of domains of social relatedness, language/communication, and restricted interest/repetitive beha-

avior are separable. They proposed that genetic and behavioral approaches that consider autism as an entity or unitary phenomenon are apt to be inefficient and counterproductive. Evidence presented in support of the fractionable approach included the smooth continua of severity seen for domain traits, the occurrence of autism-related traits in isolation in family members and the general population, the modest within-individual correlations seen for the different domains, the different developmental trajectories seen across domains, and the apparent independent heritability of the relevant traits.⁵

Although the dimensional “fractionable” approach to autistic behavior is gaining support, hard evidence is still relatively limited, and the instruments used to assess the relevant behaviors have been relatively crude. However, it can be suggested that a more nuanced and fine-grained approach would likely provide even greater support for the fractionable perspective. More generally, support for a more dimensional and “phenomic” or endophenotype approach to behavior, cognition, and emotion is gaining strength in neuropsychiatry.⁶ Such an approach seems to offer advantages in terms of metrification and from an individualistic, descriptive, and idiographic standpoint. The upcoming revision of the *DSM-IV* should offer opportunities for spirited discussion of the fundamental issues.

EMERGENCE AND AUTISM

The potential separability of autism-related traits may provide especially fruitful reductionist routes to research on autism. Many of the causative factors that are operating in autistic individuals are also probably playing a role in social, communicative, and repetitive behavior in family members and in the general population. However, at the same time that components are considered in isolation, it must be taken into account that some of the most distinctive, intriguing, and perplexing aspects of autism might arise from an interaction of the

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separable aspects or of the factors underlying these fractionable and familial traits. The possible interactions can be grouped into the simple additive, the multiplicative, and the emergent. It is the emergent phenomena that might arise from the interaction of component factors that will be considered in detail. Here, *emergent* is stringently defined as referring to phenomena that are novel and that differ in type and quality from the interacting components.

The concept of emergence can be traced to Aristotle's metaphysics, and the term itself was used by pioneer psychologist G. H. Lewes in 1874 to refer to "qualitative novelty." There was increased interest in emergence in the 1950s with the development of general systems theory and an increased study of complexity. In the early 1980s, the Sante Fe Institute was formed to investigate complex phenomena across disciplines including physics, chemistry, biology, neuroscience, and economics. There are now multiple journals devoted to the area and a number of institutes dedicated to the study of complexity. It is clear that various sorts of complex behavior can arise from simple systems like cellular automata and neural networks (see listed Web sites), and the idea that simple programs can model and apparently underlie complex physical and biological systems has been thoroughly presented by Wolfram. Systems biology is focused on comprehending how system properties "emerge" at and across the levels of the gene, transcriptome, proteome, metabolome, cell, tissue, and organism. The use of a complex systems or systems approach to pathobiology and disease classification is being championed.⁷

The term *emergensis* was introduced to the field of behavioral genetics in 1981 by David T. Lykken who used the term to refer to "...a polygenic mechanism that involves an extreme type of gene interaction. An emergent trait is one that is determined by a particular combination of genes of a number of loci, thus forming a gene 'configuration' or gene constellation. When any one gene is absent, it destroys the configuration and the emergent trait disappears."⁸ The critical nature of each component in a configuration and the often isolated (nonfamilial) nature of the phenotype were emphasized. The pattern of emergent inheritance was considered to be different from the single-locus inheritance pattern observed in many genetic diseases and from the typical polygenic inheritance of quantitative traits that are determined by additive effects of multiple loci.

Key initial questions for autism researchers are how to define and identify emergent autistic phenomena. A simple operational definition of emergent traits would be those that are not often seen in family members but that seem to arise from an emergent interaction once multiple impairments or attributes coalesce within an individual. Another closely related defining criterion would be the presence of a marked difference in correlation or concordance between dizygotic (DZ) and monozygotic (MZ) twins. An additional and more speculative criterion would be discordance or discrepancy in MZ twin pairs.

POTENTIALLY EMERGENT PHENOMENA IN AUTISM

The emergence of nonfamilial phenomena in the autistic individual is probably best represented by intellectual disability (ID). Although the familial aspects are less well studied, seizures in autism also can be nominated as being emergent. Based on their apparent comparative rarity in relatives, a number of other autism-associated phenomena deserve consideration as potentially emergent and are listed in Figure 1. These include stereotypies, self-injurious behavior (SIB), persistence of primitive reflexes, special skills, morphological, and neurochemical abnormalities, as well as sleep problems, gait disturbances/postural control, clumsiness, and brain laterality. Further careful family studies are needed in most cases to determine the extent to which particular phenomena can be considered emergent. It is remarkable (but not surprising) that most of the phenomena mentioned are not part of the necessary

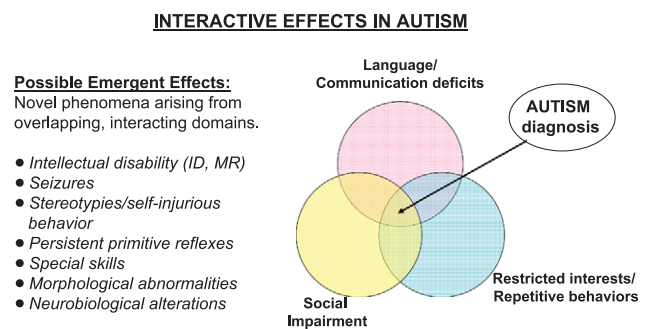


Fig. 1 Additive and multiplicative effects can increase severity when domains of abnormality overlap within an individual. The emergent model emphasizes the importance of novel phenomena that might arise from interactions among the factors underlying domain abnormality. The listed phenomena are nominated as emergent based on their apparently not being seen at above general population rates in family members of individuals meeting criteria for autism. These novel, potentially emergent, phenomena might critically depend on specific configurations of genetic and biological factors.

diagnostic criteria for autism. A more detailed and extensively referenced discussion of each potentially emergent phenomenon is available.¹

Intellectual Disability

It is generally accepted that family members of individuals with autism do not have scholastic difficulties or cognitive impairment at rates much or at all above those seen in the general population. This lack of family loading for cognitive impairment is a strong indication that the ID often associated with autism is an emergent product of interacting factors associated with autism-related phenomena. The evidence from twin studies further supports the idea that autism-related ID is non-familial (in the usual sense), as IQ is much more highly correlated in MZ twin pairs than in DZ twins, in pairs with at least one twin with autism. Although, in general, IQ is highly correlated within MZ twin pairs, large differences in IQ have been observed in some autistic MZ twin pairs. The larger than expected IQ differences might be due to a dependence of ID on a critical configuration of abnormalities or factors. Such an underlying configural cause may be sensitive to subtle cotwin differences in gene activation (epigenetics) that begin with the earliest pretwinning events of embryonic development.

Seizures

The lifetime prevalence of seizures in individuals meeting criteria for autism is approximately 33%. The rate is substantially higher in individuals with autism and ID, and there is an apparent bimodal distribution in age of seizure onset in autism. The rate of 33% is substantially higher than the general population rate of 2% to 3% and also seems to be much higher than the rate in family members. Two studies have found epilepsy to occur in parents of probands at rates seen in the general population, thus tending to support an emergent origin in autism. It should be noted that seizures do not seem to occur at above base rates in individuals meeting criteria for Asperger syndrome. This latter observation may provide clues about the combination of factors necessary for seizures to occur. Further investigation in this general area is needed to establish rates in family members, to improve estimates of concordance in MZ and DZ twins, to determine if late-onset seizures are of a special sort, and to understand better the relation of early- and late-onset seizures to ID in autism.

Stereotypies and SIB

Stereotypies and SIB are frequently reported in autism but are not a requisite part of autism spectrum diagnostic criteria. Given the often striking nature of stereotypies and SIB, it seems obvious that the behaviors do not occur to nearly the same extent or degree in relatives. However, a careful study of rates of stereotypies or of frank SIB and related self-harm behaviors in siblings, cotwins, and parents has not been performed. Determining their degree of emergence will require further clarification of the relations of the behaviors to one another, to other behaviors included in the restricted and repetitive behavior domain of *DSM-IV*, and to IQ.

Persistence of Primitive Reflexes

The remarkable persistence of primitive snout and visual rooting reflexes in children and young adults with autism has been reported.⁹ Although family members have not been studied, it seems unlikely they would show rates of primitive reflexes much above the general population. Concordance in twin pairs has not been tested.

Special Skills

Mathematical genius has been proposed as a paradigmatic example of an emergent behavior in the general population,⁸ at times appearing in individuals whose families showed little similar talent in previous or subsequent generations. Similarly, the savant skills that have been observed to occur in individuals with autism do not seem at first glance to occur in family members. However, there is some limited evidence that relatives exhibit increased rates of savant skills. A number of other less striking special abilities including heightened perception of details, hyperlexia, enhanced memory skills, and the acquisition of large bodies of knowledge can be present in autism. The familiarity of these various traits and their associated processes has been little studied.

Morphological Abnormalities

There are an increasing number of reports of early brain growth abnormality in a substantial proportion of individuals with autism. The basic finding of brain overgrowth in the first few years of life is now well replicated, although the regional specificity, relative gray and white matter contribution to the overgrowth, and

issues of laterality remain to be clarified. It is noteworthy that several recent studies indicate family members also often show macrocephaly, making it less likely that the brain overgrowth is an emergent phenomenon (as defined herein). However, other reputed neuroanatomical abnormalities might arise from such processes. Also, major congenital and minor physical anomalies have been observed to occur at elevated rates in autism, whereas rates in family members do not seem elevated.

Neurochemical Alterations

A range of neurochemical abnormalities has been reported for autism, including alterations in serotonergic, glutamatergic, GABAergic, cholinergic, and stress response systems. However, many of the observations are not fully replicated, and few have been examined in family members. Exceptions are the well-replicated platelet hyperserotonemia of autism and the related finding of reduced expression of central and peripheral 5-HT_{2A} receptors. Although platelet serotonin levels appear highly heritable, the heritability of the hyperserotonemia is less clear. 5-HT_{2A} expression does seem to be lower in family members, but data are limited. Decreased nighttime urinary excretion of the pineal hormone, melatonin, has also been replicated and would be suited to examination in relatives.

DISCUSSION

Criteria for operationally defining emergent phenomena in autism need to be established. An initial approach would be to define the degree of emergence based on the extent to which behaviors are rare in relatives and, perhaps, on the amount of discrepancy seen within the MZ twin pairs. Identifying specific phenomena as emergent should enhance their study and lead to the subsequent elucidation of the factors that need to co-occur for the phenomena to “emerge.” Many of the phenomena nominated as potentially emergent seem to be associated with, and perhaps require, substantial impairment or abnormality from across the three major domains of autistic behavior. While the present domain-based *DSM-IV* diagnostic criteria for autism define a heterogeneous group, it is a group highly enriched in individuals showing novel and nonfamilial (emergent) phenomena (Fig. 1). Individuals with impairments in

only one or two domains would provide crucial contrasts. Studies of at-risk siblings and other family studies also should be designed in a way that allows a full consideration of potentially emergent phenomena.

The genetic study of emergent phenomena can be predicted to be especially difficult because of the evanescent nature of the phenotypes, and it is probably best to avoid standard genetic approaches to such phenomena. In contrast to this cautionary note, it can be pointed out that the sensitivity of emergent phenomena to configuration offers hope in terms of behavioral and pharmacotherapeutic intervention. The potential for small changes to produce large nonlinear effects on emergent phenotypes is exciting and should provide impetus to this area of research. Future genetic, biological, behavioral, and therapeutic investigations in autism may well be guided to a large extent depending on the emergent or nonemergent nature of the trait being studied.

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WEB SITES

- <http://www.stephenwolfram.com/> (Wolfram’s book, *A New Kind of Science*, is largely, if implicitly, concerned with emergence.)
- <http://en.wikipedia.org/wiki/Conway> (An animated graphical depiction of complex behaviors emerging from simple programs.)
- http://books.google.com/books?id=E70oJWsGFsEC&dq=Mario+Augusto+Bunge&printsec=frontcover&source=an&hl=en&sa=X&oi=book_result&resnum=5&ct=result (Site offers a preview of philosopher Mario Bunge’s book, *Emergence and Convergence*, a wide-ranging discussion of the importance of emergence.)