Commentary

Autism Spectrum: New Metaphor
- New Paradigm of Illness

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This commentary reflects on the attachment of the word "spectrum" in the past decade to autism, a disorder with etiologies that have, in previous decades, been uniquely controversial – leaving parents to float between various medical opinions. Spectrum is an apt metaphor for medical thinking in which the individual, not the disease, is the target of treatment. Its use may, however, deprive patients and parents of the security offered by the conventional notion of a well defined "disease entity." The spectrum metaphor will serve medical language's aim of precision if information technology can endow its spatial meaning with detail, accuracy and structure. When given place and proximity patients' narrative and laboratory descriptions provide patients, practitioners, and researchers a collective instrument – a "macrosope" - for letting the data talk about etiology and options for treatment. "Autism Spectrum Disorder" (ASD) has entered common parlance over the recent decade. Parents of newly diagnosed children feel that their child is more lost than found by a term, *spectrum*, that lacks the precision of a diagnostic *entity*. For physicians and scientists ASD's spatial reference of "spectrum" may call attention to our lack of a system of scientific notation for capturing the many details that may be passed-by in the rush to the terminal branch of the differential diagnosis tree. Those details of medical narrative provide the basis for giving each patient a point in a conceptual space. That space differs from traditional nomenclature of disease by inviting information technology to find new ways to capture, store, analyze and report the patient's story. The author describes an invention and its application in a web-based system, Autism360.org. The system functions as a "macroscope" revealing patterns that answer questions we might not otherwise know to ask. As such it fits within the model of what has been called Fourth Paradigm Data Intensive Science and offers the potential for integration with laboratory data and expansion to practice and research in all chronic illness.
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INTRODUCTION

Autism was described by Kanner in 1942.[1] Problems with speaking, repetitive behavior and interaction with others in young children remain today its defining features. Once rare and thought to be caused by "cold" mothers, in the five decades of the author's medical career autism has become a common condition. Rimland's scholarly review of the lack of scientific evidence for psychological causes and the strong evidence fo biological causation of autism signaled a dramatic shift of opinion during the decade of the 1970's when genetic research began its ascendancy. During the past decade's controversies – at first regarding the reality of the rise in autism's incidence, and then over causation – no studies of psychological causation have entered the debate.[2] Current beliefs as to its causation from genetics to environmental and epigenetic factors: "a family of diseases with common phenotypes linked to a series of genetic anomalies, each of which is responsible for no more than 2–3% of cases. The total fraction of ASD attributable to genetic

inheritance may be about 30–40%."[3] The authors cite the 10 toxins most likely to represent the environmental exposure accounting for the remaining 60-70%. A study of twins[1] concludes that "Susceptibility to ASD has moderate genetic heritability and a substantial shared twin environmental component." An exhaustive report[5] by Andrew T. Cavagnaro, Ph.D of the California Department of Developmental Services detailed the increasing ASD caseload 1997-2007 showing a 13.4 annual increase between 2002 and 2007. In 2004 an international public/private partnership of government health agencies and private advocacy organizations committed more than $21 million for research to identify the genes associated with autism spectrum disorders.[6] To the extent that investment in research is a measure of the strength of opinion one must conclude that the scientific community has, within the past decade, embraced profoundly divergent opinions on which to base private and public decisions regarding the prevention and treatment of autism. The words "genetic predisposition" have come more into use as a picture has formed of an enormous environmental tragedy in which the vulnerable central

nervous system of the very young and very old heads the list of damages produced by exposure to bad food, air, and water. Autism has not only stood out for the remarkable and changing diversity of practice and opinion, but, in addition, has become unique in the wide acquisition of "spectrum" as a vernacular modifier of a word previously understood fully within the medical metaphor of disease "entity."

PIONEERING METAPHOR

The word "spectrum" appears to have crept into use as if our common language was presenting a reality that had not been articulated from an authoritative source. The published use of spectrum as applied to Asperger's Syndrome by Gillberg[6] in 1985 is credited as the original source. A web search of "spectrum disorder" turns up one reference to "bi-polar" among the first twenty relating to autism. A scholarly understanding that bi-polar and, for that matter all disorders, can be viewed as a continuum of symptoms is likely to propagate the metaphor. At present, however, ASD appears to have emerged from an untidy history of conflicting beliefs to pioneer a valuable metaphor.

What value is brought to the medical and scientific community with the expression "autism spectrum"? Increasing knowledge about any phenomenon usually produces incremental precision suiting the goals of public policy and clinical practice. The welcome afforded the introduction of this new term by practitioners and scientists is surprising considering well publicized contemporaneous authoritative efforts[7] to redefine autism by more specific, and narrowed, inclusive criteria. Such efforts have entailed polarization among lumpers and splitters regarding strict definitions necessary for comparative studies. The entry of spectrum to our scientific and clinical vocabulary offers consideration that Nature's strict definition of living things is a poor model for ideas we form about illness. If, however, "spectrum" is to help us find a clearer picture of autism, we may wish to find a more strict understanding of its implication.

Nowhere in publications in the field of autism or any other disease has any illustration depicted parameters by which the spatial features of spectrum might be understood. Efforts to identify sub-types of autism have so far failed to produce results compatible with the principles and boundaries of systematic taxonomy. Sir Isaac Newton's name for whites light's apparition in a colorful band revealed by a prism gives us neither scale nor boundaries within which to place a speechless child. No parent has asked me to say whether her child is of the red, orange, yellow, green, blue, indigo or violet type. Given the medical impulse to name subtypes of disease, no type I or type II of autism has emerged. Instead a vague sense of high (Asperger's Syndrome) and low function presents to parents no new information with the use of "spectrum" attached to the diagnosis given by practitioners. A diagnostic "entity" brings to the grief of a worrisome diagnosis some relief that "they know what it is." To be told that your child is in a spectrum invites a feeling that he is more lost than found.

NAMES, NOTIONS AND THINGS

"Entity" is a word sometimes used for specter or ghostly apparitions. More commonly, "entity" refers to a living or nonliving thing with distinct existence. "Disease entity" is used in medical parlance in the latter sense. That use promotes a logical fallacy. In *a critique of language in the study of medicine* F.C. Crookshank MD in Appendix II of the 1923 linguistics classic *The Meaning of Meaning*[8] warns of the mischief of confusion among happenings to individuals, the ideas we form about patterns of similar events in groups of people, and the names we give to them. Such confusion may be trivial in self-limited conditions: "Death was the result a fall from the scaffolding." "Sue missed school because of a strep throat." In both instances a real happening (fall) or entity (Strep) is named. The shift of disease prevalence from simple acute illness to complex chronic conditions has presented an unmet challenge to our language's ability to avoid a misleading metaphor for causation. Both lay and scholarly publications routinely refer to symptoms that are *caused by* schizophrenia, ulcerative colitis, or lupus erythematosis. I read Crookshank's essay in 1969 at the suggestion of my senior colleague and mentor, Shannon Brunjes MD, in the Division of Medical Computer Sciences at Yale Medical School. My way of thinking about clinical options and research was permanently altered.

Crookshank points to the failure in medical science to "distinguish between what we observe in persons who are ill, on the one hand, and the general notions we form in respect of like illnesses in different persons, together with the 'linguistic accessories' made use of by us for purposes of communication concerning the same, or the other." He defines, in other words, the fallacy introduced by the confusion of names, notions and things.

"It is not to be thought," writes Crookshank, "that any educated medical man really believes *'a disease'* to be a material thing, although the phraseology in current use lends colour to such supposition. Nevertheless in hospital jargon, diseases are 'morbid entities' and medical students fondly believe that these 'entities' somehow exist *in rebus Naturae* and were discovered by their teachers much as was America by Columbus."

After reading Crookshank I could no longer hear the words "disease entity" without cringing. Nor could I fail to feel the tension between differential diagnosis and understanding each patient as an individual. In the latter case, not only the metaphor but the fundamental principles differ from those applied to the treatment of disease.[5] Evidence based medicine defines a system of beliefs and practices with strict criteria for grouping patients and observing the group's response to test the validity of treatments. Principle based medicine begins with the fundamental fact of biology: that each living thing is unique.

CODING INDIVIDUALITY

Soon after shifting my medical compass from disease to individual, I was struck during an annual examination of an institutionalized non-verbal autistic 13 year old boy.

Ophthalmoscope in hand, I gently approached his eye. Suddenly his fist shattered the bridge of my eyeglasses, which I had inadvertently left in place. As much as I was stunned I was also awestruck by the reptilian precision and speed of his gesture. Only upon reflection did the richness of his non-verbal communication hit me. "You are looking into me, but fail to see me." That message ripened as, during the ensuing years autism changed from being a rare to common illness and I considered how Dr. Brunjes' lessons in information technology could help me see my patients' individuality while enabling the same data to talk about patterns revealing more about diseases than their diagnostic criteria. I continue to ponder how autistic individuals may be better seen, individually and collectively especially when they carry a label that implies but does not give understanding.

How could I better see and enable such a boy who caught my attention to be seen by others? My answer over the years has been a tool for building an accurate, detailed, structured record that captures patients' anonymous narrative. The primary goal is the creation of a record to share with caregivers presenting an organized portrayal of their individuality. When meeting others who we wish to know us - prospective in-laws, bosses, or a graduate school admissions officer – which of us would start with calling attention to our weakness, symptoms, quirks, or abnormal lab tests? On the contrary, our strengths and special skills would head the list. In a medical setting such positive attributes may perhaps merit at least a place among the aforementioned items. Information technology provides a way for individuals in with chronic illness, or their parents, to create a record that helps them see themselves as a sum of particularities in a format more useful than a diagnostic label, especially if the label is a "spectrum." If spectrum, moreover, is an apt concept the threads of individual portraits can find even more value in their context within an informative collective tapestry.

Precedents for such an approach to "granular data" are afoot in research models of Fourth Paradigm Data Intensive Science. Telescope-based cosmological technology and satellite-based remote imaging of Earth exemplify information technology's capacity to make sense from very large data sets. In these disciplines the "selection criteria" may be represented by a signal filter. The data is, however, accepted "as is" from its source free of selective preconceptions of the viewer. The meaning of the data is then extracted in the patterns made by the data, not by hypothesis-driven experiments. Health data is cited[i] by the pioneers of Fourth Paradigm Data Intensive Science as ripe for exploitation.

Much health data as it currently exists is, however, degraded by its having been passed not through an optical filter but by the eye of another observer. Whomever that observer may be - physician or 'coder' in a hospital or medical office - the signal that emerges is, at best, deprived of details or what we call granularity. At worst, the code is an effort to please the necessity of an insurance form, a lab requisition, a discharge summary, or death certificate, imprisoning them in anachronisms.

For the past five decades doctors have led information technologists to treat their arcane language without the kind of interchange that has characterized the use of information technology in other fields. In medicine a tacit invitation to think in new ways has been rejected in favor of automating the status quo. However information technology may have aided the many –omics of medicine, medical narrative has suffered from "codelessness" at best, or, at worst, the life support of the relics of archaic medical language. We humans have a keen eye for patterns. Information technology can help us sharpen our vision if we can capture the details that constitute the individuality of our patients, including their strengths. The extraordinary strengths and special skills of some autistic individuals may be seen for their value to our species search for adaptation to a changing environment. Their imagination, given tools for envisioning patterns, may help find solutions to clinical problems.

A MACROSCOPE

Envisioning patterns depends on having a "macroscope" permitting the grasp of otherwise invisible data-shapes comparable to those material shapes found with microscopes and telescope and other instruments for remote viewing. Such systems for visualization involve information technology at their nether end. With the collaboration of others including his patients the author's creation of a macroscope began with the encoding of the language of medical narrative. The meaning of each of more than 4000 symptoms, strengths, special skills, exposures, life events, and other descriptors was coded by a system described in more detail elsewhere.[11] The coding system's design, unlike the tree-shaped International Classification of Diseases or the Diagnostic and Statistical Manual of Mental Disorders 5 is based on a multidimensional matrix. Over a period of two decades the author encoded the meaning of words used by each of his patients to describe their illness. The intersection of System, Function and Where created a point in conceptual space that would place, for example, "itchy rash on the hand" as the intersection of System: *skin*, Function: *itching* and Where: *hand*. Modifiers quantifying severity, various temporal descriptors, aggravating and alleviating factors contributed to virtual points in a 22-dimensional space. (Baker, 2012) The pattern carries all elements of the patient's narrative. As implemented in the web application Autism360.org the user is required to enter a minimum of 15 profile items and one strength or special skill to qualify for matching to others by dot-product proximity analysis. Real-time matching produces a cluster of "others like me" providing a source of information regarding the positive, negative or neutral effects of treatment options reported by cluster mates. The individual user benefits from a sense of place in the spectrum.

The collective picture of many users is illustrated in **Figure 1**. It is the first published picture of the autism spectrum as portrayed not metaphorically but literally as the sum of narrative gathered as the free flow of data from its source: the patients.
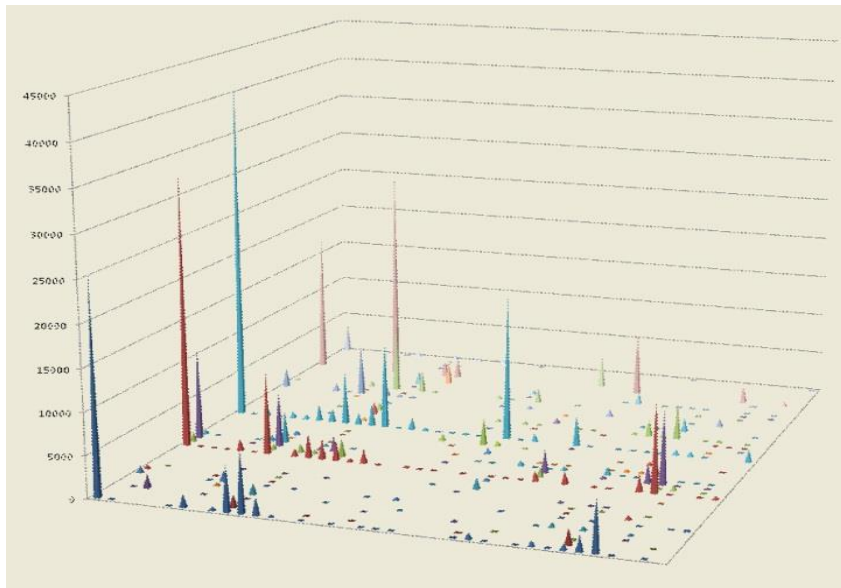
Figure 1. The Autism Spectrum in Three of Multiple Data Dimensions. 79,482 symptoms of 1,831 parent-identified autistic children ages 2-18. Shown are 286 logical intersections 38 Systems (X axis) x 41-Functions (Y axis). The vertical Z axis shows the sum of severity scores at the time of onset.

Figure 1 is presented as a glimpse of a system for observing nature akin to image of the starry sky in a telescope. Analysis of patterns revealing differences in gender and BMI has been published (Baker, 2012) and detailed interpretation of those patterns is in preparation for publication. Three of the 22 dimensions of the data acquired in 2 years of service by Autism360 to users in more than 80 countries and territories are presented here as a literal representation of "spectrum" to illustrate the potential of information technology to transform a figure of speech into a way to let the data talk.

LABELING THE ROWS AND COLUMNS
The names of the Systems and Functions not shown in the illustration. Their categories emerged from the narratives and records of my patients in my practice devoted to complex chronic illness after 1978. "System" includes the physiological and anatomical divisions of conventional terminology augmented by necessary descriptors such as Life Event, Warmth and Craving. The necessity of such 'anomalous' Systems was to find the best compromise between parsimony and completeness of an effort to capture the literal meaning of the words patients used to tell their stories. Warmth, for example, became a System because symptoms of heat, cold and thermal instability arise frequently. Warmth, moreover, is a quality for which the "Functions" "Increase" and "Decrease" apply. The project began with rows and columns on paper, a pencil and the key technology of an eraser with no rules except to capture as closely as possible the most practical literal meaning of the patients description of symptoms and other elements of narrative that ultimately became referred to as 'profile items.' Any rules, as such, developed in the course of the project. The ninety-ten rule – that the majority of symptoms are expressed in a fraction of the collective lexicon – came into play as I replaced paper with computer where dropdown

menus could ease the capture of common symptoms and free time to ponder novel items. It became clear that a sparse matrix would necessitate obligatory elements (System, Function, Where) to serve as the meaning's anchor, from which modifiers could be floated as appropriate. The application of this invention[3] changed in the course of two decades from explorative phases, to a computer based system for in-office gathering of patients' narratives to a web-base system for patient-entered data. The final rules were to permit a level of detail that satisfied the patient's need to tell the whole story, to have immediate feedback for verification, and to create and effectively own a record the anonymity of which absolutely protects confidentiality. As the search for efficiency and structure of the system progressed, every effort was made to bar the exclusion of "outlier data" by giving users equal access to unusual as to common descriptive items. In the creation of Autism360.org a concession was made to its major funder that the system created, up to that point to handle the entire lexicon of chronic illness be trimmed and tailored to suit the interests of the global autism community. Thanks to the support of The Moody's Foundation and other funders, the Autism360.org is free to its users.

The "high altitude" picture of Autism360's data without labels provides a novel view of a disease. Analysis now published and more under way, the growth of Autism360, the addition of laboratory data, and the expansion beyond the fuzzy margins of the autism spectrum may further enrich our view of chronic illness. A glance at **Figure 1** suffices to defy the notion that defining problems with speech, behavior and interaction describe the extent of its features. See the blue peak at the center of the grid. It lies at the intersection of Immune (System) and Increase (Function) carrying a variety of words relating to abnormally increased immune (broadly

re-defined) response to environmental exposures. That peak says that autistic children are sensitive in that way just as they are – as seen in other parts of the data – to sensory (sound, light, taste, touch, smell) stimuli. One may thereby reflect that the immune system is, after all, a sensory apparatus. Joining sensory and immunologic phenomena in our picture of autism gives us a better picture of where to look in investigating children individually and collectively.

SUMMARY
The development and application of the system described here has heeded the Aristotelian advice "to look for precision in each class of things just so far as the nature of the subject admits."[13] Language is messy and rendering it into rows and columns cannot sharpen its point. It can however give us access to meaning on a new scale of independence from the limits of a single tale or a given tongue. The mother tongue of many readers of this essay no doubt treats human health with metaphors less misleading than the way the author has represented "entity." In the last decade English has presented its speakers with the novel widespread use of spectrum as a modifier of a "specific disease." Science depends on a precision of language often offered by deliberate consensus. Spectrum's stealthier entrance into our vocabulary on the back of autism is, in the opinion of the author, likely to spread. Such a spread will at best be by way not simply of a loose metaphor but by a grasp of the real details that provide proximity or distance among individuals who carry the same diagnostic label. The reality that it represents when portrayed in multidimensional frame of thinking and information technology is shared by all chronic illnesses no matter how well defined they may be. If symptoms, strengths, lab tests, quirks and curious features survive the process of labeling the individual, they may provide new vistas when given an organized place in a private medical record as well as anonymous representation in collective data. If details beyond the bounds of diagnostic criteria are preserved in the record we may optimistically predict that the word "spectrum" will become attached to many diseases in common parlance, not limited to statistical research. Clinical focus on the individual as the target of treatment may find the lens of the macroscope described here useful for envisioning

a collective picture permitting new ways of thinking about chronic illness. That new way will reveal the value of data that gives emphasis to commonalities – oxidative stress, problems in detoxification, inflammation[14] – among chronic illnesses and reveals shared etiologic factors.

CONFLICT OF INTEREST
None.

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